FACTORS INFLUENCING END-OF-LIFE MORBIDITY:

AN EPIDEMIOLOGICAL EVALUATION OF POPULATION AGING THEORIES

by

Mini Elizabeth Jacob

MBBS, Christian Medical College, Vellore, India, 1997

MD, Christian Medical College, Vellore, India, 2005

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This dissertation was presented

by

Mini Elizabeth Jacob

It was defended on

March, 30, 2015

and approved by

Steven Albert, Ph.D.
Professor, Department of Behavioral and Community Health Sciences
Graduate School of Public Health, University of Pittsburgh

Robert M. Boudreau, Ph.D.
Assistant Professor, Department of Epidemiology
Graduate School of Public Health, University of Pittsburgh

Mary Ganguli, M.D., M.P.H.
Professor, Department of Psychiatry and Neurology, School of Medicine
Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh

Janice C. Zgibor, Ph.D.
Associate Professor, Department of Epidemiology
Graduate School of Public Health, University of Pittsburgh

Dissertation Advisor and Committee Chair: Anne B. Newman, M.D.,
M.P.H. Professor and Chair, Department of Epidemiology
Katherine M. Detre Endowed Chair of Population Health Sciences
Graduate School of Public Health, University of Pittsburgh

Anne B. Newman, MD, MPH

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ABSTRACT

Population aging theories were proposed to explain the effect of an increasing life expectancy on the duration of the morbid period at the end of life. Despite several decades of research, the epidemiological basis of these theories has not been investigated adequately. This dissertation uses data from the Cardiovascular Health Study, a community based cohort of older adults, to explore the epidemiologic basis of the basic tenets of these theories.

Hospital stay at the end of life is an economically important measure of terminal morbidity. We examined the effect of lifestyle factors measured late in life on the duration of hospital days in the last 5 years of life. We found that alcohol consumption, smoking, obesity and social networks were independently associated with hospital stay, indicating that a late-life lifestyle could impact end-of-life morbidity after accounting for the accumulated disease burden.

Cardiovascular mortality rates have been falling but it is not clear whether the morbidity associated with these events have reduced. We compared the risks for disability and death associated with cardiovascular events and found that angina, MI, CHD and CHF had stronger

associations with death than disability. Cardiovascular events, therefore, do not seem to increase the disability burden in the population.

The relationship between age at death and the duration of terminal morbidity has not been elucidated in community based populations with average life expectancy. We examined the association between age at death and the length of terminal self-rated poor health and found that survival is associated with the duration of end-of-life morbidity in a curvilinear fashion; morbid period is shorter for those who die in their seventies and nineties. Identifying factors that promote survival to the nineties would help delineate factors associated with a compressed period of morbidity.

What are the public health implications of these findings? First, some preventive health behaviors can be harnessed to reduce the public health burden of terminal morbidity. Second, chronic diseases with low mortality risk need to be targeted to reduce the disability burden in populations. Third, survival to the nineties might hold the key to compressing morbidity in the older population.

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PREFACE

This dissertation is dedicated to the memory of my father, the late Professor. P.U. Jacob, whose passion for learning and pursuit of excellence continues to inspire me seventeen years after his death.

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1.0 LITERATURE REVIEW

1.1 POPULATION AGING THEORIES

James Fries, in his ground breaking article in the New England Journal of Medicine in 1980, propounded the compression of morbidity hypothesis.[1] Fries argued that the maximal lifespan was around 85 and the natural limit to lifespan would prevent any further increases in life expectancy. He further stated that, as most premature deaths were being caused by chronic diseases in late life, and as these diseases could be postponed by changes in lifestyle, morbidity could be compressed into a shorter span between the increasing age at onset of disease and the fixed limit of lifespan. In his later papers, Fries defined his hypothesis more comprehensively to state that compression of morbidity would occur if the age at first appearance of disease was increasing more rapidly than life expectancy.[2, 3]

Fries' compression of morbidity paradigm was a stark and optimistic contrast to the expansion of morbidity theory proposed by Ernest Gruenberg in 1977.[4] In his article "The Failures of Success", Gruenberg stated that the successes of modern medicine and public health have resulted in prolonging life with advanced degenerative disease, as a result of which people are spending more time in advanced disease and disability. Both these theories were challenged by Kenneth Manton, who proposed a third theory, the "theory of dynamic equilibrium" in 1982.[5] He proposed the alternative scenario where an increase in prevalence of chronic diseases would be

counter-balanced by a decrease in the severity of these diseases. This would lead to an increase in years with morbidity but the years with severe morbidity and disability would remain relatively constant.

The different theories contradict each other essentially because of their differing views on what causes the increase in life expectancy or the 'delay' in death at older ages.[6] The expansion of morbidity theory explains the 'delay' in death by highlighting the effect of modern medicine in preventing fatal outcomes due to degenerative disease. The 'delay' occurs in the final stage of progression of chronic disease i.e., from severe disease to death. This theory implicitly assumes that the age at onset of disease remains unchanged. It relegates the role of primary prevention in postponing disease and delaying the degenerative processes of disease to postpone severe disease and disability. On the other hand, the compression of morbidity theory implies that preventive behaviors are at the forefront in preventing disease and death. These behaviors 'delay' the onset of disease as well as death but the 'delay' in onset of disease is greater, i.e. their effect in postponing disease is greater than their effect in postponing death. This theory relies on the plausibility of primary prevention by lifestyle factors. In contrast to both these theories, the theory of dynamic equilibrium highlights the 'delay' in progression of disease from less severe to more severe diseased states. In this scenario, health promoting behaviors as well as clinical medicine would result in slowing disease progression in early phases resulting in a prolonged phase of mild disease. Figure 1.4.1 demonstrates this in graphical form.

These theoretical discussions pertaining to the different theories of population aging need to be validated by epidemiological analysis of observed data. The important questions that emerge when one desires to test these theories in epidemiological studies and surveys is (1) How should morbidity be measured for the purpose of testing for compression/expansion of morbidity? (2)

What is the best method for demonstrating compression/expansion of morbidity in populations? The aim of this paper is to review current literature to comprehensively answer these questions and identify why epidemiologic research has failed to provide a consensus regarding these theories. In this process, three potential research questions will be identified, the answers to which will fill gaps in the literature pertaining to these theories of population aging.

1.2 MEASUREMENT OF MORBIDITY FOR TESTING POPULATION AGING THEORIES

1.2.1 Potential measures for estimating morbidity

A crucial factor that needs to be considered when population aging theories are to be tested is how morbidity is to be estimated in older populations. The two overarching possibilities are to define morbidity as presence of chronic disease or as presence of disability. From the above discussion on population aging theories, it seems logical that the selection of the index should be based on its association with longevity. If longevity is associated with escape or delay in chronic disease, the morbid period should be measured in terms of chronic disease. Instead, if longevity seems more strongly associated with escape from disability, then the morbid period should be measured as the period of life with disability. Studies among the longest lived provide evidence whether this population has delayed disease and disability.

In a case series of 32 super centenarians (age 110 to 119 years) from the New England centenarian Study (NECS) in the US by Schenhoefen et al, 41% required minimal assistance or were independent. There was a very low prevalence of vascular disease including myocardial

infarction (n=2) and stroke (n=4). Although Diabetes was rare (n=1), hypertension (22%), osteoporosis (44%) and cataract history (88%) were common. The authors concluded that functional independence and absence of vascular disease seemed to be dominant characteristics of exceptional aging. [7]

In a study of 207 Danish centenarians, 52% were found to be hypertensive, 10% were diabetic and 72% had cardiovascular disease (which included moderate hypertension and anti-hypertensive treatment). Only one subject was free of any chronic condition. This study identified 41% of the centenarians to be relatively independent in spite of having a similar number of co-morbidities.[8]

Evert et al described the morbidity profiles of all centenarians in NECS in terms of being 'survivors' (centenarians diagnosed with at least one common age-related condition before age 80), 'delayers' (centenarians who were diagnosed with at least one disease at or after the age of 80) and 'escapers' (centenarians who reached 100 years of age without the diagnosis of any of the common age-related diseases). The presence or absence of the following age-associated conditions was used to determine morbidity profiles: hypertension, heart disease, diabetes, stroke, non-skin cancer, skin cancer, osteoporosis, thyroid condition, Parkinson's disease and chronic obstructive pulmonary disease. 38% were survivors, 43% were delayers and 19% were escapers. The authors state that these different centenarian phenotypes indicate that there are different pathways to longevity. Although a certain number of centenarians may reach their age by avoiding or delaying age related diseases, a significant number actually cope with disease.[9] Using a similar definition to define survivors, delayers and escapers, a study of 188 centenarians in Australia showed that 46% were survivors, 35% were delayers and 19% were escapers.[10]

Another research paper from NECS attempted to disentangle compression of morbidity from compression of disability.[11] Of 739 centenarians in the study, 32% were survivors, i.e. , they developed morbidity (chronic obstructive pulmonary disease, dementia, diabetes, heart disease (defined as myocardial infarction, arrhythmia, and congestive heart failure), hypertension, osteoporosis, Parkinson's disease, or stroke) before 85 years and 68% were delayers, i.e., they did not develop these conditions until after 85 years. Survivors and delayers for each chronic disease did not show a significant difference in independence in terms of Barthel Index scores except in the case of diabetes where survivors had a significantly lower median score than delayers of diabetes. These data suggest that compression of disability and compression of morbidity are different phenomena. The delayers exemplify compression of morbidity where they compress chronic diseases to the very end of their long lives. The survivors include people who have compressed disability without compressing morbidity. Compression of disability is therefore possible without a compression of morbidity.

Ailshire et al, in an analysis of data from the Health and Retirement Study compared disease and functioning trajectories among 1045 respondents who died before reaching 100 and 96 participants who survived to their 100th birthday. Centenarians were found to have fewer diseases and fewer ADL limitations at every age but the trajectories of cognitive function were found to be similar. It was found that although centenarians were in general healthier, there was considerable heterogeneity in their pathway to longevity. About 53% were 'survivors', about 23% were 'delayers' and 24% were 'escapers'.[12]

To summarize, studies among centenarians have varied results but in general, suggest that heterogeneity is the most plausible characterization of the centenarian experience. There are different trajectories to longevity in terms of escape from disease and also multiple phenotypes in

terms of both physical function and disease burden. Therefore different measures of morbidity need to be considered for evaluating population aging theories.

1.2.2 Disability as a measure of morbidity

Disability has been the most commonly used measure of morbidity in research evaluating population aging theories. There are several other reasons why disability is an attractive measure of morbidity in old age. Disability is a good measure of the overall health status in older adults who might have complex disease patterns which cannot be quantified precisely. Disability status is very often measured in studies of older adults and is easily obtained by self-report. Disability is a sequel to many other measures of morbidity – subclinical disease, clinical disease, frailty and self-rated health. Being an outcome measure of all these other measures makes it an attractive measure of morbidity in its later stages. Also, disability has direct implications to the long term care needs of older adults, a major source of health care expenditure at the personal and public level. Testing for compression/expansion of disability is therefore pertinent from a financial perspective.

On the other hand, there are certain disadvantages in using disability alone for measuring morbidity. Aging and disease affect the body in a dynamic fashion and disability represents only one phase, the penultimate one, in this process. The costs and damage incurred in disease states before the development of disability could be substantial.[13] To test population aging theories comprehensively, several phases of the process has to be tested including subclinical disease, mild and severe disease states. The theory of dynamic equilibrium suggests that the phase of severe disease will be compressed but the phase of mild disease will expand. This indicates that for testing aging theories, measures of milder disease may need to be used along with measures of

severe disease. Measuring disability in terms of functional limitations and IADL and not just ADL measures, and including performance measures may be a way to expand the spectrum of morbidity which is captured by the disability construct. Another limitation of disability measures is that they are measured by self-report and therefore tends to be influenced by environmental conditions. This may prevent its comparison across cultures and countries.

Another major issue with the use of disability as a measure of morbidity is lack of a universal definition of disability across studies. Disability has most often been measured using self-report of difficulty with Activities of Daily Living or ADL (eating, dressing, bathing, walking around, transferring, and using the toilet) and tasks required for independent living called the Instrumental Activities of Daily Living or IADL (preparing meals, shopping, housekeeping, managing money, taking medications, and using the telephone). Katz proposed six basic ADLS in 1963 which have been the basis for assessment of disability for the past several decades. The original list has been modified over time and different surveys and studies often pick and choose items. The wording of questions and responses are often modified which prevents comparison across studies. Researchers may prefer self-report of difficulty to a self-report of dependency depending on the research question being addressed. A disadvantage of the scale is that subtler degrees of disablement are not captured. In a population of older adults, often only 10 to 15% of the population will have ADL difficulty. The functional status of the remaining 85% will remain undifferentiated.[14] Older adults with functional decrements, who compensate or adapt and therefore do not perceive difficulty, will not be identified if we use the ADL scale alone. Questions pertaining to IADL and functional limitations capture minor degrees of functional loss by self-report. Self-report of functional status uses questions pertaining to pulling or pushing, lifting weights, reaching, handling small objects etc.

Self-report of disability has inherent limitations. Responses depend heavily on how questions are asked and response categories are worded. The time interval mentioned in the question can have an impact on the response as there is often short term change in functioning. Questions may ask for current status or status over a certain time in the past; the latter may capture more disability. Questions may also ask for actual performance of a task versus capacity to perform a task. An activity may not be performed but that does not indicate that the individual is incapable of performing it. On the other hand, a report of capacity does not indicate that the individual is actually performing the task as he or she may not have attempted to do it recently.

Performance measures were developed to objectively assess function, in the background of growing concern that self-report of functioning and disability may not be accurate. They exclude the effect of environment which may affect the self-report of disability. They allow for accurate assessment of trends in physical function by negating the influence of changing environments. They also facilitate comparison across countries and cultures as cultural perceptions and differential access to assistive devices does not affect the measurements. The pegboard test, picking up object, lifting 10 pounds, gait speed, chair rise (single and repeated) and stair climb are performance tests which assess a single task. The timed up and go test combines chair rise and gait speed requiring the participant to rise from a chair, walk 10 feet and then return to the chair. The Short Physical Performance Battery (SPPB) includes 3 components - the side by side, semi-tandem and tandem stands each held for 10 seconds, the 4 meter walk at usual pace and the single chair stand followed by five timed chair stands as quickly as possible. The SPPB score has been found to predictive of subsequent hospitalization,[15] disability,[16] nursing home admission and mortality.[17] In individuals without disability, a lower SPPB score was predictive of ADL and mobility disability one and five years later.[16] This implies that this objective measure of lower extremity

functioning is able to identify pre-clinical states of disability in older individuals. Gait speed by itself is a powerful predictor of mortality among older adults and performs almost as well as the full battery in predicting incident disability.[18] Improvement in usual gait speed has shown to predict a substantial reduction in mortality.[19]

To summarize, different measures of disability and function measure different domains and use a variety of methods. When disability is used to measure morbidity in studies testing population aging theories, the domain and the severity of disability being measured has to be kept in mind, so that one has a clearer understanding of the level of morbidity being measured.

1.2.3 Hospitalization as a measure of morbidity

Research has mostly focused on hospitalizations among older adults as a measure of healthcare utilization. Measures of hospitalization, which include admission rates and length of stay could be used as a measure of the duration of severe morbidity among older adults. Hospitalizations have been consistently associated with the burden of chronic disease.

Another reason why hospitalizations could be a morbidity measure of particular interest is the cost involved in elderly hospitalizations. Older adults are known to be disproportionately greater users of hospital services. Although they constitute only 12% of the population, older adults are responsible for 35% of hospitalizations and 44% of the national hospital bill.[20] Healthcare expenditures for older adults are increasing at a faster rate than the spending for the rest of the population. This is partly due to the aging of the population and partly due to the increase in spending by older adults themselves.[21] This can lead on to an unprecedented strain on Medicare. Collection of hospitalization and cost data of Medicare beneficiaries makes it possible for analysis of large samples.

Also, hospitalizations are important events in the functional trajectories of older adults. They can lead to life threatening complications unrelated to the admitting diagnosis including delirium, falls, nosocomial infections and pressure sores[22, 23] and can propel older persons into a state of irreversible functional decline.[23] The number of days in the hospital can therefore be a useful measure of the duration of a severely diseased state and also an indicator of future morbidity.

1.2.4 Self-rated 'poor health' as a measure of morbidity

The study of self-rated health has evolved into a large body of literature over the last three decades. The use of self-rated health became popular in the early eighties as psycho-social epidemiology emerged as an important field. This variable is variously termed perceived health, subjective health, global health, self-reported health etc. It is assessed using a single question which may differ slightly from study to study but in general, asks the participant to rate their own health. The global nature of the question is implicated by asking 'In general" or 'All in all'. The concept included in self-rated health seems to be insensitive to the semantic variation in the question assessing it. It also appears to over-ride technical difficulties involved in translation to other languages.[24]

One of the most important reasons to use self-rated health as a measure of morbidity is its strong association with mortality. Self-rated health predicts mortality even after adjusting for other health variables including function. Studies have usually demonstrated odds ratios of 1.5 to 3 but one study has shown an odds ratio as high as 93.5.[25] Idler and Benyamini evaluated 27 longitudinal studies from the US and around the world that showed an impressive association between self-rated health and mortality after accounting for health status.[24] They have also considered various interpretations which can account for the association. They propose that self-rated health is a more

inclusive and accurate measure of health status, risk factors , trajectory of health, health behaviors and even the family history of health and illness.

Self-rated health is also a valid proxy for objective measures of health status. It has been shown to be associated with 43 diseases among men and 31 diseases among women.[26] Singh-Manoux et al investigated the factors determining self-rated health in two European cohorts. In the Whitehall-2 study, five determinants (symptom score, sickness absence, longstanding illness, minor psychiatric morbidity, number of recurring health problems) explained 34.7% of the variance in self-rated health. In the Gazel study, four measures (physical tiredness, number of health problems in the past year, physical mobility, number of prescription drugs used) explained 41.4% of the variance in self-rated health.[27] In the Cardiovascular Health Study, self-rated health has been used to develop the Years of Healthy Life measure, which is defined as the number of years in the study during which the participant reports good, very good or excellent health. Years of Healthy Life has been shown to be associated with physical activity,[28] depression[29] and Brain MRI findings.[30]

Self-rated health has not been previously used as a measure of morbidity in the testing of population aging theories before. The strength of its association with health and mortality and the feasibility and acceptability of this measure in studies of older adults should place this on par with disability measures for estimating morbidity.

1.3 EPIDEMIOLOGICAL METHODS IN THE TESTING OF POPULATION AGING THEORIES

1.3.1 Indirect methods of testing population aging theories

If the duration of the morbid or disabled period in individuals undergoes a change, this will be reflected in a change in the mean duration of this period in populations. This should in turn, change prevalence rates of disease and disability in populations if the age composition of the population remains constant. Trends in disability rates among older Americans have been used by researchers to make conclusions about population aging theories. Table 1.4.1 summarizes results from the major studies which undertook the analysis of disability trends in the US. Three of these studies are described below.

A major source of information was the National Long Term Care surveys (NLTCS). Manton et al analyzed data from the NLTCS from 1982 to 2004/2005 and found a significant rate of decline in chronic disability.[31] Disability status in the NLTCS is defined using information on ability to perform 8 instrumental activities of daily living (IADLs: light housework, laundry, meal preparation, grocery shopping, getting around outside, getting to places outside of walking distance, money management, and using the telephone) and 6 activities of daily living (ADLs: eating, getting in or out of bed, getting around inside, dressing, bathing, getting to the bathroom, or using the toilet). For a person to be ADL-disabled in the NLTCS, it was necessary that the person report that the activity "had not been performed, or was not expected to be performed, without the aid of another person or the use of equipment for at least 90 days." A person was I ADL-disabled if he or she "could not perform one of the IADLs for 90 + days because of disability or health problems". Disability was classified into light to moderate levels of disability (only

limitations of IADL and up to 4 ADLS) and severe disability(five or more ADLS or institutional residence) and concluded that there was a decreasing trend in both light to moderate and severe disability.

Seeman et al assessed disability trends among US adults aged 60 or more using 2 National Health and Nutrition Examination Surveys in 1988-1994(n=4688) and 1999-2004(n=4239).[32] They measured ADL disability with 4 questions, IADL disability with 3 questions mobility disability with 2 questions and functional limitations with 3 questions. Disability in each domain was defined as the report of some or greater difficulty in 1 or more relevant items for that disability. This study reported significant increases in each type of disability for all except the oldest.

Schoeni et al used data from 1982 to 2002 National health Interview surveys to assess disability trends. [33] The NHIS includes a sample of 8000 adults aged 70 and older among whom disability was assessed using two questions. The first question asked whether participants required help for ADL. If they answered no to this, they were asked whether they needed help for IADL. This study reported that declines were substantial in terms of IADL disability but ADL disability did not show much change.

All three studies mentioned above are on nationally representative samples and assessed disability trends during the same time period but gave contradicting results. Survey designs and analytic decisions, small changes in composition of the sample in terms of age, gender, race and education can have huge effects on the estimates. Also, changes in wording of questions, number of questions and definition of disability can have major effects on estimates of disability burden.

An influential review of the major studies by Freedman et al in 2002 provided a consensus by stating that there were considerable declines in ADL IADL disabilities and functional

limitations across studies.[34] A more recent analysis of data seems to indicate that the decrease in prevalence rates may have come to an end.[35]

1.3.2 Direct measurement of the disabled period in populations

Population aging theories focus on the magnitude of morbidity experienced by older adults in their lifespan, towards the end of their life. Estimating this involves longitudinal measurement of morbidity indicators in a population and aggregating it to represent morbidity. This is very often not feasible other than in cohort studies of older adults with long follow up. As life expectancies started increasing and multiple aging theories were proposed, the need to answer questions regarding the health of aging populations became evident. In 1984, the World Health Organization pioneered the development of survival curve models to explain the consequences of increasing survival on the health status. [36] Disease free and disability free life expectancies were calculated by extending the regular life tables to include morbidity and disability. A few years later, the International Network on Health Expectancy and the Disability Process or REVES [Re´seau d'Espe´rance de Vie en Sante´] was created to facilitate international collaboration in health expectancy calculations. This agency examines trends in health expectancies in different countries to make conclusions regarding compression and expansion of morbidity.

Active Life Expectancy (ALE), the most commonly calculated health expectancy is the mean number of years a person is expected to survive in an active state, i.e., free of any disability. It is an aggregate measure of life spent without disability and is hence an attractive measure to test population aging theories. ALE can be calculated using the Sullivan Method, the double decrement life table method or the multi-state life table (MSLT) method. The Sullivan method combines the age specific mortality from the period life table with age specific prevalence of

disability from survey data[37] whereas double decrement and MSLT methods are based on population transition rates, e.g., disability incidence and recovery rates. There has been concern that the Sullivan's method may have potential biases and limitations in tracking changes over time as it uses prevalence rates (which are affected by previous health states of the population including incidence, recovery rates and mortality rates)but there is evidence that biases are small when transition rates are changing slowly over time.[38] This method is of practical importance because it uses readily available data, is simple and easy to interpret.[39]

The MSLT method (also called the increment decrement method) uses longitudinal person level data on transitions in disability status to develop estimates of first order Markov transition probabilities. As it allows transitions to and from disability it is considered superior to the Sullivan method for estimating Active Life Expectancy. It is also considered superior to the double decrement method in which the disability state is considered to be irreversible. Age and gender specific probabilities of transitions then used to simulate the paths of older adults to disability and death. This is done by applying the transition probabilities to artificial cohorts of 65 year olds. The transition rates are assumed not to change with time, hence the experience of a 65 year old in 15 years will be the same as that of a 80 year old at the time when transition rates are estimated. Also, possible future changes in age composition are not considered. The number of transitions is limited to one per interval which is unrealistic. Total Life Expectancy (TLE), Active Life Expectancy (DLE) and Disabled Life Expectancy (DLE) are estimated from simulated lifetime trajectories.[40] Active Life Expectancy calculated at different time points can be used to track changes and test population aging theories.

Multi state life table methods are arguably the best method to calculate Active Life Expectancy but as noted, it makes several assumptions which are unlikely to be true. Moreover,

ALE is a surrogate for what the population aging theories actually predict i.e., the actual number of years in active and disabled states that older adults pass through. Rarely, in cohort studies of older adults, this data becomes available and can be used for testing population aging theories. In the Cardiovascular Health Study, after 18 years of follow up of 5888 older adults, Years of Able Life (YAL)[41] which indicates the number of years without any ADL difficulties, has been calculated along with the total number of observed years (Years of Life or YOL) and the disabled years and provides a unique opportunity to test the theories of population aging. Years of Able Life can be termed as the 'observed' version of Active Life Expectancy. It is a robust measure of healthy survival, incorporating health as well as longevity. It takes into account recovery from disability.

1.3.3 Current evidence regarding population aging theories

Despite considerable research over the past 30 years, there has been no consensus on the experiences of populations in recent years in terms of the duration of the 'morbid period' at the end of life. Research evaluating evidence for these theories has not given consistent results not only due to the diverse methods in which morbidity is measured and but also because of the diverse research methods used to provide evidence. Table 1.4.2 gives a brief description of studies which have attempted to test the compression of morbidity hypothesis using different methods.

The compression of morbidity has been tested by estimating ALE using nationally representative data in the US[40, 42-46] and in other countries. [40, 47, 48] Some of these studies are described in detail below.

Cai and Lubitz applied multi state life tables to data from the Medicare Current Beneficiary Surveys (MCBS) conducted from 1992 to 2003.[49] The MCBS has a rotating panel design and

follows each individual for 4 years. The study sample consisted of 43891 Medicare beneficiaries aged 65 and older. Based on responses to 6 ADL and 6 IADL questions, participants were characterized to have four mutually exclusive disability states – Active health(No ADL or IADL disability), IADL disability(disabled in at least 1 IADL but no ADL disability), moderate ADL disability (disability in 1 or 2 ADLs) and severe ADL disability(disabled in at least 3 ADLs). Age and gender specific probabilities of disability transitions were calculated for consecutive years from the observed data using multinomial logistic regression. These were applied to an artificial cohort of 500,000 65 year olds and TLE, ALE and DLE were obtained. TLE increased by 0.5 years from 1992 to 2002 and ALE increased 0.8 years. A small insignificant decrease in DLE was attributable to severe ADL DLE; moderate ADL DLE and IADL DLE did not change. The age of onset of disability remained fairly stable and yet it was observed that all the gains in TLE were in ALE. It was therefore inferred that recovery from disability was playing a major role in increasing ALE. The authors concluded that the findings supported compression of morbidity except for the increases in TLE (Fries had predicted that life expectancy would not increase further).

Crimmins and Beltran-Sanchez reviewed research and survey data in the US in 2010 to make conclusions regarding the existence of a compression of morbidity.[50] They examined trends in incidence rate and mortality due to major chronic diseases causing mortality (heart disease, stroke, cancer, diabetes) stating that trends in these conditions should underlie any compression of morbidity. They state that incidence rates for MI, stroke and cancer have not changed, while survival has increased. Incidence, prevalence and age adjusted death rates due to diabetes have increased. The authors cite these as evidence regarding the worsening health of the population. They also used the Sullivan method to calculate healthy life expectancy related to four major chronic diseases and mobility functioning. Prevalence rates (based on self-report) were available

from the National Health Interview Survey and mortality rates were obtained from the US official life tables. They demonstrated that life expectancy without CVD, cancer or diabetes as well as life expectancy with mobility functioning ability has decreased from 1998 to 2006.

Few studies have looked at compression of morbidity using longitudinal data. Vita et al used data collected from University of Pennsylvania alumni to study the effect of lifestyle factors on cumulative disability.[51] Alumni aged between 63 and 72 years in 1986 were surveyed seven times using mailed health assessment questionnaires between 1986 and 1994. The study included 1741 highly educated men and women; 77% were men and 99% were white. The predictors considered included BMI, smoking, exercise and chronic conditions. Subjects were assigned to risk strata (high, moderate and low) based on BMI, smoking and exercise. A health assessment questionnaire assessed difficulty in 8 activities of daily living and the scores were averaged across the activities and summed over the 7 assessments to calculate a cumulative disability index. There was a significant increasing trend in cumulative disability scores from low risk group to high risk group. The authors noted that their study was the first to examine the relationship between health risks and total lifetime disability.

Hubert et al analyzed data from the University of Pennsylvania alumni reducing the sample to 418 participants who had died. [52] This study used a different method to test for compression. Spline regression models were fit to disability over time in each risk group. Slope of disability at an earlier segment was compared to the slope of segment closest to death. The hypothesis was that healthier lifestyles would lead to delayed acceleration in functional decline before death. The results showed that those with healthier lifestyles had less overall disability and no acceleration in functional decline before death. Those with two or more risk factors reached a greater level of disability earlier in life and also experienced an earlier acceleration.

Andersen et al analyzed data from the New England Centenarian study to test for possible compression of morbidity among centenarians (age 100-104 years), semisupercentenarians (age 105-109 years), and supercentenarians (age 110-119 years).[53] One hundred and four supercentenarians, 430 semisupercentenarians, 884 centenarians, 343 nonagenarians, and 436 controls were followed for an average of 3 years. The study found that with increasing age, the later the onset of chronic diseases, as well as of cognitive and functional decline. The hazard ratios for individual diseases became lesser with age, and the relative period of time spent with disease was lower with increasing age group. There was a progressive delay in the age of onset of physical and cognitive function impairment, age-related diseases, and overall morbidity with increasing age. The authors concluded that, as the limit of human life span was effectively approached with supercentenarians, compression of morbidity was generally observed.

Using data on Years of Able life in the Cardiovascular Health Study, we tested for compression of morbidity due to lifestyle factors (unpublished). Multiple lifestyle factors were assessed at baseline including smoking, alcohol consumption, physical activity, BMI, diet, social networks and social support, and Activities of Daily living (ADL) were assessed at baseline and throughout follow-up. Years of Life (YOL) was defined as observed years till death or 18 years, and years of Able Life (YAL) was defined as observed years without any ADL difficulty. We examined the association of each lifestyle factor with YOL, YAL, and the YAL/YOL fraction using separate linear regression models that adjusted for confounders. Multiple lifestyle factors were significantly associated with the observed total and able years of life as well as the proportion of observed life lived without disability. Smoking was associated with a loss of able years. Greater physical activity, higher intensity of exercise, longer distances walked, better diet quality, and better social supports were associated with a relative compression of the disabled period. Obesity

was associated with a relative expansion of the disabled period. At comparable values of socio-demographic factors, a healthy lifestyle differed considerably from an unhealthy lifestyle in terms of YAL, YOL, disabled years and YAL/YOL% and was associated with an absolute and relative compression of the disabled period in all race and gender groups (Figure 1.4.2).

1.3.4 Gaps in the literature on evidence for population aging theories

The review of literature on population aging theories and the evidence regarding them has brought out several gaps. Firstly, there is a lack of consistency among researchers regarding how to define and measure morbidity for the purpose of testing population aging theories. A primary cause of the lack of clarity regarding trends in disability is the use of different disability measures in different studies. There is no consensus as to what constitutes disability in research studies. While some measure difficulty in ADL and IADL, some measure dependency while others measure functional and sensory limitations. It is important to demonstrate the differences in the magnitude of estimates of burden and risk of disability when these multiple definitions are used. Also, there is a clear need to go beyond the disability based definition and include other measures of morbidity.[54]

Secondly, there is a lack of consensus on what compression of morbidity entails when national level data are examined. The compression paradigm considers morbidity as a lifetime cumulative area under the curve concept rather than cross sectional event.[55] According to this hypothesis when the onset of morbidity is postponed to a greater extent than postponement of death, the average burden of illness per individual is reduced. This could lead to a reduction in the national burden of illness. At the same time, the growing number of older persons is increasing the national burden of disease. Therefore trends in prevalence, incidence or mortality rates due to

a disease in the population will not give a complete picture and can only provide supportive evidence for compression or expansion. At the national level, compression can be clearly established by comparing trends in age specific disability rates (surrogates for the less easily quantitated morbidity rates) with trends in age specific mortality. If age specific disability is declining faster than age specific mortality then compression is occurring.

In epidemiologic studies of older adults, the best way to demonstrate compression is to examine serial cohorts of longitudinal data and assessing trends in cumulative lifetime disability. This is logistically and financially a difficult endeavor. Assessment of trends in Active Life Expectancy come close to capturing compression or expansion but is a considerably limited method when compared to having actual observed data from cohorts. Multi-state life tables provide period based estimates and not cohort based estimates. They do not reflect the experience of cohorts through time. Studies that have examined longitudinal data to assess cumulative disability are sparse and have been restricted by small sample sizes, lack of generalizability of findings and deficiencies in capturing a comprehensive set of lifestyle factors and confounders.

Thirdly, researchers have focused on testing overall compression without examining the processes which could make compression of morbidity a possibility. There is a dearth of literature regarding the potential for lifestyle factors in compressing or expanding the morbid period. A basic tenet of the compression of morbidity hypothesis is that healthy lifestyle factors can postpone the onset of morbidity and compress the morbid period. But apart from the two studies mentioned previously there has not been any attempt to measure the ability of lifestyle habits to compress this period. A lack of availability of longitudinal data which capture end of life morbidity is the main reason why there has not been much research in this area.

Another epidemiologic question that has not been answered adequately is about the effect of chronic diseases on the morbid period. Population based studies of older adults have demonstrated associations between specific diseases and disability.[56-59] Studies have also demonstrated that with increasing number of chronic disease conditions, there is a step wise increase in ADL, IADL and mobility disability.[60] Fried et al studied interactions between diseases and the type of disability they caused in the Women's Health and Aging study and found that interaction between diseases were significantly associated with disability rather than isolated diseases by themselves. The type of disability that disease caused varied depending on the presence of another disease.[61] This was a cross-sectional study. There is no observed data regarding the duration of disabled period associated with individual chronic disease or multimorbidity. It is important to understand how chronic disease influences disability free survival and overall survival and to disentangle and compare the effects on both. This is particularly important in the case of cardiovascular disease, the leading cause of death among adults in the US. The disability data from CHS provides a unique opportunity to study the relationship between cardiovascular disease (well documented in CHS) and the disabled period.

A third research question that needs to be addressed is basic question of the effect of survival on the morbid period in representative populations. Although there is evidence that centenarians compress the period of disability[11], there is a lack of information on how a longer duration of life among individuals in the general population, is impacting the disabled period. It is important to quantify the average number of disabled years an older adult who lives to 95 might experience compared to the number that a person who survives to 75 or 85 might experience. This information is important to individuals and institutions due to its economic implications.

These questions are different from the broader demographic question of whether compression/expansion of morbidity is occurring in populations, yet these are important epidemiologic questions which need to be answered in order to explore the process of compression/expansion in individuals. These questions parallel the broader demographic question and help explain and predict population level changes.

1.4 TABLES AND FIGURES

Table 1.4.1 Studies evaluating trends in disability rates among the US older adults population

Author(Year)	Data source	Measurement used	Major finding
Manton et al (1997)[62]	NLTCS 1982 -1994	ADL, IADL	Any disability:↓ (24.9% to 21.3%) ADL :↓(13.1 % to11.9%) IADL: ↓ (5.6% to 4.3%)
Manton et al (2001)[63]	NLTCS 1982 -1999	ADL, IADL	Any disability:↓ (26.2% to 19.7%) ADL :↓(13.6 % to10.6%) IADL: ↓ (5.7% to 3.2%)
Manton et al (2006)[31]	NLTCS 1982 to 2004/2005	ADL, IADL	Any disability:↓ (26.5% to 19.0%) Mild to moderate disability (upto 4 ADL) :↓ (15.5 % to11.8%) Severe disability (5+ ADL):↓ (11% to 7.2%)
Crimmins et al (1997)[64]	NHIS (1982 to 1993) Longitudinal Study of Aging (1984,1986,1988,1990)	ADL, IADL	Any disability:↓ (22.7% to 20.2%) ADL :remained level IADL: ↓ (14.5% to 13.8%)
Schoeni et al (2001)[65]	NHIS (1982-1996)	ADL, IADL	Any disability:↓ (22.7% to 19.3%) ADL :remained level

Table 1.4.1 Continued

			IADL disability:↓ (14.5% to 10.9%)
Schoeni et al (2005)[33]	NHIS (1982-2002)	ADL, IADL	Any disability:↓ (22.7% to 15.5%) ADL: remained level IADL disability:↓ (14.5% to 8.1%)
Freedman et al (1998)[66]	Survey of Income and program participation (1984 to 1993)	Functional Limitations	Any difficulty: lifting and carrying:↓ (23.5% to 18.9%) Climbing a flight of stairs: ↓ (34.9 to 31%) Walking a quarter mile :↓ (37.6 to 31.5%)
Freedman et al (2000)[67]	Supplements on Aging (1984 to 1995)	Functional Limitations	Difficulty with upper body limitations: ↓ (5.1 to 4.3%) Difficulty with lower body limitations :↓(34.2% to 28.5%)
Liao et al (2001)[68]	Supplements on Aging (1984 to 1995)	ADL IADL Functional Limitations	ADL disability: ↑ (12.5% to 14.8% in men,16.9% to 18.6% in women) IADL: no change Functional limitations: ↓ Lot of difficulty or inability to perform tasks declined from 34.3% to 31.2%

Table 1.4.1 Continued

Waidmann et al (2000)[69]	Medicare Current Beneficiary Survey	Functional Limitations	Functional Limitations: ↑(23.5% to 25.2%)
Fuller-Thomson et al (2009)[35]	American Community Survey (2000-2005) National Nursing Home Survey(2004)	ADL Functional Limitations	ADL : ↑9% Functional limitation: stable
Seeman et al(2010)[32]	NHANES (1988-1994 and 1999-2004)	ADL, IADL, Mobility limitation Functional limitation	Increasing levels of all types of disability except in those aged>80

Table 1.4.2 Studies which directly tested the Compression of Morbidity hypothesis

Author (Year)	Data Source	Method	Major Findings
Bernstein et al (2004)[70]	Case study	Disease profile and autopsy of an Okinawan-Japanese centenarian	Delay/escape from age associated diseases indicate compression of morbidity
Parker et al (2005)[71]	SWEOLD 1 and 2 Sweden (1992, 2002) (National surveys among population aged 77+, includes institutionalized)	Prevalence Adjusted Odds for Year 2002	ADL, IADL: No change Mobility limitation: ↑ Health problems: ↑ Concludes that there is no compression of morbidity
Liu et al (2009)[72]	National Disability Surveys China (1987, 2006)	ALE (Sullivan Method)	ALE (At age 60):↑ from 13 to 13.9 ALE (at age 90): ↑ from 1.2 to 1.5 Proportion of DLE with sever disability decreased, least disability increased Onset of disease delayed from 0.3 to 4.7 years
Jiawiwatkul et al (2012)[73]	National Health Examination Surveys Thailand (1997, 2004)	ALE (Sullivan method)	ALE (men): ↑ (16.5 to 17.6 years) ALE (women): ↑ 17.9 to 19.9 Women had more years with disability
Graham et al (2004)[47]	Social indicatory Survey (1981) Disability survey (1996) New Zealand	Health Expectancy (Bayesian analysis)	Expectation of years with moderate mobility and agility limitations. No increase in major limitations.

Table 1.4.2 Continued

			Concluded that the theory of dynamic equilibrium fits new Zealand.
Doblhammer et al (2001)	Microcensus surveys 1978,1983,1991,1998 Austria	Healthy Life Expectancy Sullivan method	Healthy Life Expectancy increased significantly over the study period.
Mamun et al (2004)	The Framingham Heart study	Disease free Life expectancy (Multi state Life Tables)	Smoking shortens life free of CVD and duration of life with CVD
Hessler et al (2003)[74]	H70 Longitudinal Study of Aging Sweden	Average number of hospital days in the last year of life (Linear Regression)	The oldest had the shortest number of hospital days in the last year of life. Concluded that this gives partial support to the compression of morbidity theory.
Crimmins and Saito (2001)[43]	NHIS 1970,1980,1990	Healthy Life Expectancy Sullivan Method	Compression of morbidity among those of higher educational status. Expansion of morbidity among those
Wang et al (2002)[75]	13 year prospective study of 370 members of a runners club	Linear mixed models and survival analysis	Runners club members postponed disability by 8.7 years compared to controls
Cai and Lubitz (2007)[40]	MCBS 1992-2003	ALE Multistate Life Tables	ALE: ↑ (0.8 Years)
Crimmins and Beltran Sanchez[49]	Multiple sources for disease incidence and mortality data NHIS	Incidence rates and mortality rates of major chronic diseases Disease free Life expectancy using Multistate life tables	Incidence of chronic disease has increased but survival is more. Disease and disability free life expectancy has reduced.

Table 1.4.2 Continued

Nusselder et al (2000)[76]	Globe Study(Netherlands) Longitudinal study of Aging(US)	DFLE, LED Multistate Life Tables	For nonsmokers DFLE: ↑ (2.5 years for men,1.9 years for women) LED: ↓ (0.9 years for men,1.1 years for women) Eliminating smoking will compress disability.
Vita et al (1998)[50]	UPenn Alumni study	Cumulative disability	Healthy lifestyle was associated with lower cumulative disability scores
Hubert et al (2002)[51]	UPenn Alumni study	Spline regression models fit to disability over time. Slope of earlier segment compared to later segment.	Those with healthier lifestyles had no acceleration in functional decline before death
Murray and Lopez (1997)[77]	Global Burden of Disease Study	DFLE DALE Sullivans method	Expectation of class I disability: 6.5 years(developed countries) 14.7 years (Sub-Saharan Africa, Expectation of class II disabilities: 8.5-18.4 years. DFLE class I disabilities at birth:9.9 years(sub-Saharan Africa) 47.7 years(women in developed countries)
Andersen (2012)[52]	New England Centenarian Study	Hazard ratio for disease and disability Age at onset	Centenarians delay the onset of disease and disability

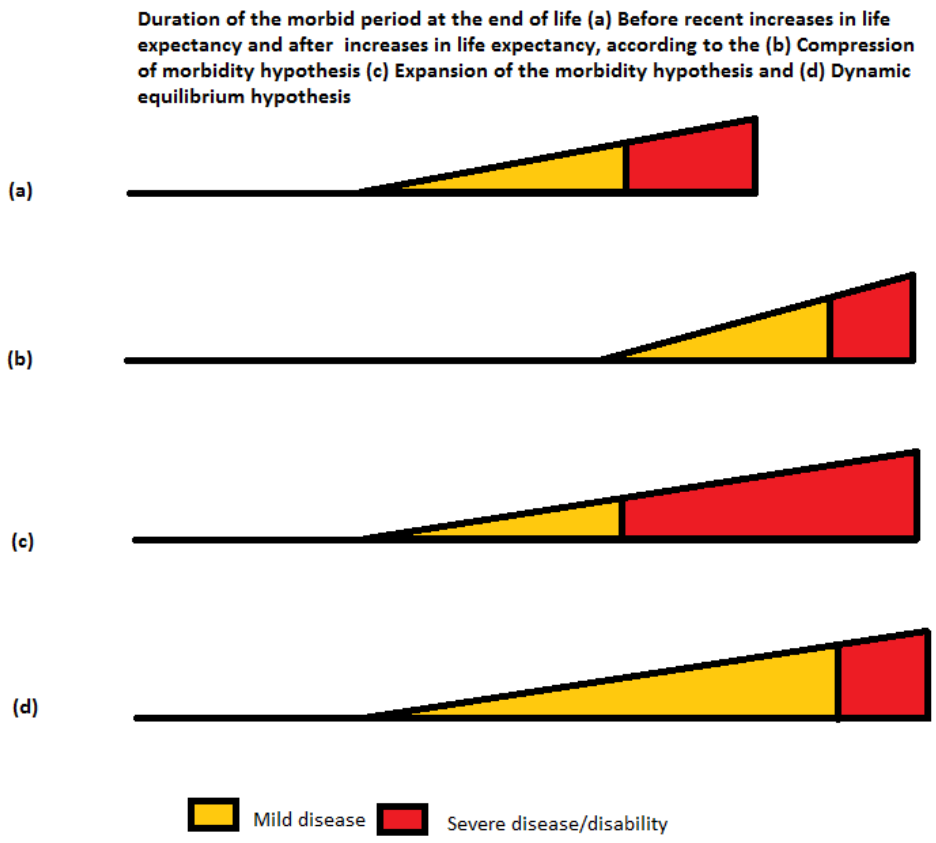

Figure 1.4.1. Duration of the morbid period (mild and severe disease) (1) before current increases in life expectancy and according to (2) the compression of morbidity hypothesis (3) the expansion of morbidity hypothesis and (4) dynamic equilibrium hypothesis

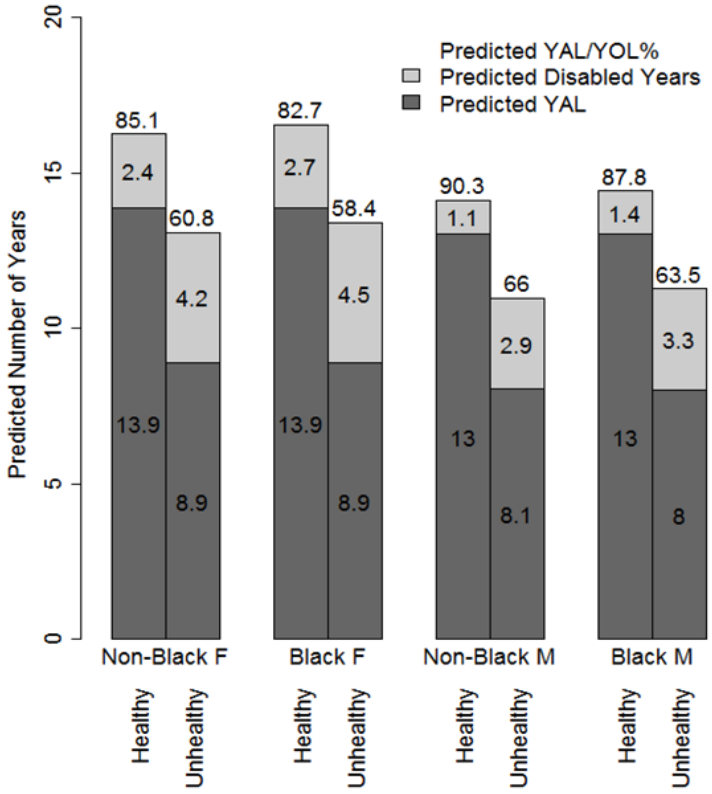

Figure 1.4.2 Predicted number of years of YAL, YOL, and YAL/YOL% for "healthy" and "unhealthy" lifestyles in different race and gender groups

2.0 LIFESTYLE FACTORS AND HOSPITALIZATION DAYS AT THE END OF LIFE

Mini E. Jacob, MD[1]; Robert Boudreau, PhD[1]; Jason Sanders, MD, PhD[2,3]; Alice Arnold, PhD[4]; Janice Zgibor, PhD[1]; Steven Albert, PhD[5]; Mary Ganguli, MD, MPH[1,6]; Anne B. Newman, MD, MPH[1]

[1]Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA; [2]Brigham and Women's Hospital, Boston, MA; [3]Massachusetts General Hospital, Boston, MA; [4]Department of Biostatistics, University of Washington, Seattle, WA;

[5]Department of Behavioral and Community Health Sciences, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA; [6]Department of Psychiatry and Neurology, School of Medicine, University of Pittsburgh, Pittsburgh, PA;

2.1 ABSTRACT

Background: While there is strong scientific evidence that a healthy lifestyle among adults can delay the onset of disease and preserve physical function, it is not clear whether a late-life lifestyle can continue to impact future morbidity. This would be important evidence for planning public health interventions among older adults. In this study, we aimed to answer the following question – Would lifestyle factors among older adults impact hospital days at the end of life, after accounting for the accumulated chronic disease burden?

Methods: We examined data from 3780 participants who died in the Cardiovascular Health Study. Lifestyle factors (alcohol consumption, smoking, body mass index, physical activity in kilocalories, blocks walked per week, exercise intensity, body mass index, diet and social networks) were measured at baseline. Hospital records were extracted to confirm hospitalizations reported by participants. Total hospital days were calculated by summing hospital days during the five years before death. Ordinal logistic regression models were used to test the association between lifestyle factors and quintiles of hospital days, adjusting for socio-demographic factors, health factors and age at death.

Results: Lifestyle factors were strongly associated with hospital days in bi-variate analyses but the effects were attenuated after adjusting for health status at baseline. Factors which were independently associated with hospital days after adjusting for confounders included alcohol consumption (1-6 alcoholic drinks/week - 22% lower odds), current smoking (34% higher odds), obesity (28% higher odds) and a higher social network score (16% higher odds for a 10 point increase).

Conclusions: Our findings suggest that late-life lifestyle factors, particularly alcohol consumption, smoking, obesity and social networks can influence hospital stay at the end of life, after accounting

for the accumulated disease burden. Lifestyle interventions like smoking cessation and obesity prevention may reduce end-of-life morbidity. The overall weak association of lifestyle factors with hospital stay indicates that this outcome is mostly determined by disease burden at this age.

2.2 BACKGROUND

Adults over 65 comprised 12% of the population the US in 2003 but accounted for 34.7% of the hospitalizations and 43.6% of the national hospital bill.[62] Combined with the rapid growth rate of the older adult population, this disproportionately high consumption of health care resources will create an unprecedented strain on Medicare.[63] Moreover, hospitalizations can lead to life threatening complications unrelated to the admitting diagnosis, including delirium, falls, nosocomial infections, and pressure sores.[31] This can propel older persons along a trajectory of irreversible functional decline, a worse trajectory than before hospital admission.[64] These factors have stimulated considerable research on hospitalizations among older adults including observational studies evaluating factors predictive of health service use [78] and interventional studies aiming to reduce hospital bed use.[79]

Health and functional status are the most commonly identified factors that predict hospital use. Frailty is associated with hospitalizations in many observational cohorts including the Cardiovascular Health Study[80-82]. Increased risk of hospitalization with the occurrence of multiple geriatric conditions has also been reported.[83] Both the number of existing chronic conditions[83-86] and difficulties in activities of daily living[83, 85] have been consistently associated with higher hospital use. Poor subjective health is also an indicator of greater use of health services.[85, 87] Depression[88] has been associated with an increased length of stay, and loneliness[89] has been associated with increased rate of hospitalizations.

In contrast to these clinical factors, lifestyle factors have been poorly studied in association with hospital stay. Although healthy lifestyle factors are linked to lower rates of chronic disease[90, 91] and mortality[92, 93], these outcomes are imperfect surrogates for healthcare utilization outcomes. Studies which do examine the association of lifestyle factors and healthcare

use mostly focus on a single health behavior, like physical activity, and have provided contradictory results.[94, 95] A recent study has evaluated multiple lifestyle factors and their impact on preventable hospitalizations among older adults but did not have adequate data to adjust for multiple chronic conditions and disability, potential confounders and/or mediators.[96] Moreover, many of these studies have been limited in sample size and duration of follow-up. End-of-life hospitalizations, in particular, have not been evaluated.

The Cardiovascular Health Study (CHS), with its comprehensive assessment of lifestyle, chronic disease, function, hospitalizations, and mortality over twenty years, provides unique data on a large cohort of community-based older adults to examine the aforementioned associations. We aimed to assess the effect of multiple lifestyle factors measured late in life on the duration of hospitalization in the last five years of life among participants in CHS. We hypothesized that healthy lifestyle factors would be associated with a reduced number of days at the hospital in the end of life, after adjusting for socio-demographic and disease related confounders. By adjusting for existing disease conditions and physical function, we would be able to estimate the independent effect of a late-life lifestyle on the duration of severe morbidity at the end of life (as measured by hospital days), accounting for the presence of an accumulated disease burden.

2.3 METHODS

2.3.1 Study design and participants

The Cardiovascular Health Study (CHS) is a longitudinal study of cardiovascular risk factors in 5888 adults aged 65 and older at baseline. Participants were recruited from a random sample of age-eligible Medicare beneficiaries and household members in four US communities: Sacramento County, California; Forsyth County, North Carolina; Washington County, Maryland and Allegheny County, Pennsylvania.[97, 98] Eligible participants were not institutionalized or wheelchair dependent, did not require a proxy for consent, were not under treatment for cancer at the time of enrollment and were expected to remain in their location for at least three years. The study enrolled 5201 participants in 1989-1990 and added 687 African-Americans in 1992-1993. Participants provided written informed consent and the protocol was approved by the institutional review boards at each participating center.

Participants completed an extensive interview and examination at the field centers at baseline. After enrollment, participants were seen annually, and were contacted by telephone at 6-month intervals until 1999. Since 1999, participants have been contacted every 6 months by telephone to ascertain health status including cardiovascular events, hospitalizations, disability, and deaths. This analysis considers follow-up through December 2011. We included 3780 participants in CHS who had died by this date and had complete data on hospitalizations.

2.3.2 Hospitalization days

Self-reported hospitalization, admission and discharge dates were confirmed by obtaining medical records. Medicare utilization files were searched to ascertain that hospitalizations were not missed. When deaths were identified at 6 month contacts, from obituaries, medical records, proxy interviews, and death certificates, medical records were extracted to update hospitalization information. Total hospitalization days were calculated by summing the days admitted for each hospitalization during the five years prior to death.

2.3.3 Lifestyle factors

Lifestyle factors were assessed at baseline and included smoking, alcohol consumption, leisure time activity, distances walked, dietary habits, body mass index (BMI), social support, and social networks. Smoking and alcohol consumption were self-reported. Participants were considered to be former alcohol drinkers if they were non-drinkers at baseline and reported 1) having stopped alcohol consumption in the past five years and/or 2) ever drank five or more drinks of any kind of alcohol almost every day. Leisure time activity (kilocalories/week) was assessed using the modified Minnesota leisure-time activities questionnaire,[99] and a weighted sum of kilocalories expended in physical activity was calculated. The highest intensity of reported activity was used to categorize the exercise intensity of participants to high, moderate, low or none.[100] Distances walked were assessed by self-report of blocks walked in the previous week. Dietary habits were assessed for the original cohort alone using the picture-sort National Cancer Institute food frequency questionnaire.[101] The Alternate Healthy Eating Index (AHEI) was calculated from this data consistent with previous studies.[102] Standardized techniques were used to measure height and

weight. BMI was calculated as weight in kilograms divided by the square of height in meters. Social support was measured using a six-item version of the Interpersonal Support Evaluation List,[103] and social networks (size, closeness and frequency of contacts) were measured using the 10-item Lubben social network scale.[104]

2.3.4 Potential confounders

Potential confounders were selected on the basis of their known association with both lifestyle factors and hospitalizations.

Socio-demographic factors: Age, gender, race, number of years of education, income, and marital status were self-reported at baseline. For this analysis, race was categorized as white and black. Non-black minority participants (n=18) were included with whites for the analysis. Education was categorized as ≤8 years and >8 years. Income was classified as ≤$25,000 and >$25,000. We also apriori decided to adjust for the clinic site as it could potentially influence both lifestyle factors and hospital days.

Health factors: Activities of Daily Living (ADL) were self-reported in six domains (eating, bathing, toileting, dressing, getting out of bed or chair, and walking around the home); Instrumental Activities of Daily Living (IADL) were also self-reported in six domains (telephone use, shopping, preparing food, performing light household work, performing heavy household work, and managing finances). Participants were categorized as having or not having any difficulty in any of the domains of ADL (ADL difficulty) and IADL (IADL difficulty). Subjective health was self-reported and participants were categorized as those reporting poor health and those reporting better than poor health. Cognition was measured using the Mini Mental Status Examination[105] and categorized as severe cognitive impairment (0 - 17), moderate impairment (18-

23), mild impairment (24-26) and normal (>27). Hypertension was confirmed if self-report was accompanied by medication use or if the average seated blood pressure was ≥140/90. Diabetes was defined as fasting glucose ≥110 mg/dl or use of anti-glycemic medication. Angina, myocardial infarction, heart failure, peripheral artery disease, stroke, and transient ischemic attack were identified using self-report and hospitalization records.[106] COPD was defined as self-reported asthma, bronchitis or emphysema. Depression was assessed using the 10-item version of the Center for Epidemiologic Studies Depression Scale and participants were categorized as depressed (≥ 10) or not depressed (<10) .[107] Missing values for baseline variables were imputed as described previously.[108]

Age at death: Age at death was calculated from the date of birth and the date of death. By adjusting for age at death, we intended to adjust for the higher survival associated with healthy lifestyle factors (which could potentially influence hospital days) and thereby obtain their direct effect on hospital days.

2.3.5 Statistical Analysis

Hospital days, the outcome variable, was categorized into quintiles because of its skewed distribution. We performed descriptive analysis by examining the distribution of lifestyle and confounder variables among participants in different quintiles of hospital days. The Chi-square test for trend was used to compare proportions and the non-parametric Kruskal-Wallis test was used to compare means in the different categories. Ordinal logistic regression models were created in a step-wise fashion to test the association between lifestyle factors and the duration of hospitalization, adjusting for confounders. In the first step we generated a core model containing socio-demographic factors. As a second step we added health status variables to the core model.

As a final step we additionally adjusted for age at death. All analyses were conducted using SAS 9.3. All statistical tests were 2 sided. The proportional odds assumption was tested using the score test. If the score test was significant, we used graphical methods to examine whether the logits were parallel.

2.4 RESULTS

Out of 3780 participants who had died, the mean age at death was 86.1 years and 42.8% were men (Table 1). Table 2 describes the baseline characteristics of these participants according to quintiles of hospital days in the last 5 years of life. Multiple variables demonstrated bi-variate associations with hospital days. Participants at the University of California Davis clinic site had significantly fewer hospital days compared to the other three clinic sites. Blacks and those with an annual income ≤$25,000 had significantly more hospital days at the end of life when compared to whites and those with higher income, respectively. Among health status variables, ADL and IADL difficulty, poor self-reported health, history of angina, MI, CCF, diabetes, PAD and depression were associated with more hospital days in bi-variate analysis. Among lifestyle variables, smoking and higher BMI were associated with more hospital days, current alcohol consumption and a healthy diet were associated with fewer hospital days, and there was a trend of fewer hospital days with higher physical activity.

Table 3 shows the results of multi-variate analysis for the lifestyle variables. In model 1, the core model adjusting for socio-demographic and lifestyle variables, alcohol consumption was significantly associated with fewer hospital days. Compared to non-drinkers, participants who consumed alcohol had lower odds of being in a higher quintile of hospital days. The association

was partially attenuated by adjusting for health factors in model 1. The association between 1-6 drinks per week and hospital days persisted in the full model; those consuming alcohol at this rate had a 21% lower odds of being in a higher quintile of hospital days when compared to those who did not consume alcohol. Other categories of alcohol consumption were not associated with hospital days.

Former and current smokers had significantly greater odds of being in a higher quintile of hospital days when compared to non-smokers. This association was slightly attenuated with the addition of confounders into the model but continued to be significant in the fully adjusted model. Current smokers had 13% higher odds while former smokers had 12% higher odds of being in a higher quintile of hospital days when compared to non-smokers.

None of the three physical activity variables were found to be significantly associated with hospital days in any of the models. BMI was a significant predictor of hospital days. In the final model obese participants demonstrated 32% higher odds of being in a higher quintile of hospital days compared to a normal weight participant. Being overweight or underweight was not associated with hospital days in this analysis. The diet score and social support score were not associated hospital days in our analysis. A higher social network score was significantly associated with more hospital days after adjusting for all confounders.

2.5 DISCUSSION

We examined the effect of lifestyle factors measured late in life on the number of hospital days in the last five years of life among deceased participant in the Cardiovascular Health Study. We found that moderate alcohol consumption (1 to 6 drinks per week) was significantly associated with

fewer hospital days while smoking, obesity and stronger social networks were significantly associated with more hospital days. The associations of other lifestyle factors, namely physical activity, diet and social support, were mostly attenuated by confounding factors.

Previous studies testing the association between alcohol consumption and hospitalizations among the elderly have found that alcohol consumption could be harmful,[96] protective[109, 110] or harmless.[111] Our finding that moderate alcohol consumption might be beneficial in reducing hospital stay at the end of life might be a result of the protective effect of alcohol in coronary heart disease.[112] It is also possible that there is some unmeasured confounding in this association; moderate alcohol consumption may be associated with better health or even a higher socio-economic status not captured by the income variable.

We found that bigger social networks are associated with more hospital days. There is conflicting evidence regarding the association between social networks/social support and hospitalizations among older adults.[113-115] Further evaluation is necessary to see whether social networks increase the risk of avoidable admissions.

We defined physical activity in three different ways and found no independent association between any of these and the number of hospital days in the last five years. Literature on physical activity and hospitalization among older adults has been inconsistent regarding the existence of this association. Physical activity had no impact on the likelihood of hospitalization[85, 94] or the duration of hospital stay[94] in some studies whereas others found that it impacted the length of stay.[95] Walking more than 120 minutes per week was associated with decreased emergency room visits and hospital stay over the next one year.[116] Many of these studies have methodological issues including small samples and residual confounding.[117] Based on the findings from our larger

sample, from a model that adjusted for multiple confounders, we conclude that physical activity among older adults does not have an independent effect on hospital days at the end of life.

Obesity has been associated with health care utilization.[118] Some studies have supported the obesity paradox in their findings of a protective association between obesity among older adults and fewer hospitalizations. Studies of post-operative outcomes have shown that obesity may be associated with an increased length of stay after surgery among older adults. Other studies have reported a J shaped association between Body Mass Index and hospitalization risk,[119] while some have reported no association.[120] Our finding that obesity and hospital stay at the end of life have a significant association after adjusting for chronic diseases indicates that obesity has an independent direct effect on hospital stay and not just an indirect effect through an increased risk for chronic disease.

The overall weak association of lifestyle factors late in life with hospitalization days is not entirely unexpected. For participants in their seventies, lifestyle has already had a substantial impact on the burden of chronic disease they carry at this age, as evidenced by literature linking lifestyle and chronic disease. At this point in life, those who have healthy lifestyles also have a lower chronic disease burden. Once disease status is adjusted for, the effect of lifestyle factors lessens. This also indicates that lifestyle change at this age is probably too late to have an effect on hospitalization, which at this point is mostly determined by the magnitude of chronic disease burden. Lifestyle changes, if needed, should be made at an earlier age when they can postpone the onset of chronic disease.

Our study has several strengths including a large sample size, longitudinal data on a community based sample, and the availability of a wide variety of lifestyle factors and confounders. We had complete follow-up on mortality and reliable data on hospital days. Our

analysis is limited in terms of behavioral and environmental measures that are known to have an impact on health service utilization among individuals. Although behavioral patterns could largely depend on socio-demographic characteristics and may be correlated with lifestyle, there may be unique individual differences in health beliefs, knowledge, and attitudes towards health services that impact decisions regarding health service use.[121] Also, adjusting for clinic site may not fully adjust for community resources that are available and accessible at an individual level. The average age at study entry was 73 and the average age at death was 86 which indicates a mean gap of 8 years between the assessment of lifestyle and the beginning of the assessment of hospitalizations. It is possible that changes in lifestyle and chronic disease burden during this period may bias results.

In conclusion, moderate alcohol consumption, smoking, obesity and strength of social networks are independently associated with end of life hospital days in this study, indicating that late-life lifestyles could impact terminal morbidity, after adjusting for the accumulated disease burden. The overall weak independent effect of lifestyle on hospital days indicate that a healthy lifestyle at this age reflects favorable socio-demographic and health factors, which in turn have the stronger associations with the outcome. Lifestyle, probably, has an earlier role in the causal pathway as a causal agent for chronic diseases which in turn are the greater determinants of hospitalizations.

2.6 TABLES

Table 2.6.1 Baseline characteristics of 3780 CHS participants who died during follow-up

Characteristic	Mean (SD)	Median (IQR)
Age at baseline	73.2 (5.4)	72 (8)
Age at death	86.1 (5.9)	86.2 (8.1)
Years of education	12.2 (3.2)	12 (3)
BMI	26.7 (4.7)	26.2(5.6)
Drinks/ week(n=3746)	2.7 (12.2)	0 (1.3)
KCals expended/week	1765.5 (2068.9)	1075.7 (1999)
Blocks walked/week	40.0 (55.9)	18 (42)
AHEI(n=3360)	39.0 (13.4)	38.5 (19)
Social Network score	32.2 (7.4)	33 (10)
Characteristic	N (%)	
Men	1617 (42.8)	
Black	522 (13.9)	
Currently married	2352 (69)	
Education ≤8 years, n (%)	596 (15.8)	
Income≤$25,000, n (%)	2381 (63)	
Current smoking	474 (12.5)	
High to Moderate exercise intensity	1643 (43.5)	

Table 2.6.2 Baseline characteristics of 3780 CHS participants according to quintiles of hospital days in the last 5 years of life

Baseline Characteristics	**Quintiles of hospital days (range)**					**P value**
	1 (0-5)	**2 (6-12)**	**3 (13-21)**	**4 (22-38)**	**5 (39-419)**	
n	812	737	719	782	730	
Clinic, n (%) Bowman Grey	186 (22.9)	173 (23.5)	188 (26.2)	228 (29.2)	219(30.0)	<0.0001
Davis	255 (31.4)	257 (34.9)	219 (30.5)	183 (23.4)	85 (11.6)	
Hopkins	192 (23.7)	152 (20.6)	145 (20.2)	176 (22.5)	214 (29.3)	
Pittsburgh	179 (22.0)	155 (21.0)	167 (23.2)	195 (24.9)	212 (29.0)	
Men, n (%)	344(42.4)	297 (40.3)	304 (42.3)	335 (42.8)	337 (46.2)	0.2485
Black, n (%)	89 (11.0)	104 (14.2)	101 (14.1)	106 (13.6)	122 (16.7)	0.0296
Age at baseline, mean (SD)	73.4 (5.6)	73.2 (5.4)	73.3 (5.1)	73.1 (5.4)	73.0 (5.3)	0.4685
Median (inter-quartile range)	72.5 (8.0)	72.0 (8.0)	73.0 (8.0)	72.0 (8.0)	72.0 (7.0)	

Table 2.6.2 Continued

Age at death, mean(SD)	87.2 (6.1)	86.6 (5.9)	86.4 (5.6)	85.6 (5.7)	84.5 (5.7)	<0.0001
Education ≤8 years, n (%)	126 (15.5)	102 (13.8)	104 (14.5)	129 (16.5)	135 (18.5)	0.1155
Income≤$25,000, n (%)	506 (62.3)	429 (58.2)	432 (60.1)	503 (64.3)	511 (70.0)	<0.0001
Married, n (%)	520 (69.2)	461 (70.0)	450 (69.1)	480(68.2)	441 (68.5)	0.9622
Any ADL difficulty, n (%)	51 (6.3)	49 (6.7)	43 (6.0)	66 (8.4)	85 (11.6)	0.0001
Any IADL difficulty, n (%)	166 (20.4)	173 (23.5)	178 (24.8)	218 (27.9)	241 (33.0)	<0.0001
Poor self-reported health, n (%)	181 (22.3)	160 (21.7)	161 (22.4)	212 (27.1)	243 (33.3)	<0.0001
Smoking, n (%) Never-smoker	394 (48.5)	339 (46.0)	335 (46.6)	349 (44.6)	292 (40.0)	0.0321
Former smoker	329 (40.5)	306 (41.5)	293 (40.8)	344 (44.0)	325 (44.5)	
Current smoker	89 (11.0)	92 (12.5)	91 (12.7)	89 (11.4)	113 (15.5)	
Current Alcohol consumption, n (%)	429 (53.1)	400 (54.7)	361 (50.9)	381 (49.4)	284 (39.2)	<0.0001
BMI, mean (SD)	26.4 (4.7)	26.6 (4.8)	26.8 (4.6)	26.8 (4.6)	27.2 (5.1)	0.0056

Table 2.6.2 Continued

Physical Activity in Kcals, mean (SD) Median (inter quartile range)	1829.5 (2172.9) 1114.4 (2078.1)	1805.0 (2103.3) 1075.7 (1952.8)	1783.9 (1877.4) 1189.9 (1896.0)	1755.6 (2055.7) 1114.4 (1918.7)	1651.6 (2092.8) 896.9 (1907.7)	0.0063
Blocks walked last week, mean (SD) Median (inter quartile range)	41.6 (58.3) 20.0 (54.0)	41.8 (56.7) 20.0 (50.0)	41.3 (53.9) 21.0 (50.0)	39.0 (53.9) 15.0 (42.0)	36.2 (56.4) 12.0 (36.0)	0.0003
Moderate or high exercise intensity, n (%)	368 (45.3)	309 (41.9)	336 (46.7)	350 (44.8)	280 (38.4)	0.0101
Alternate Healthy Eating Index, mean (SD) Median (inter-quartile range)	40.1 (13.3) 39.5 (20.0)	39.9 (13.2) 39.5 (19.0)	39.5 (13.4) 39.5 (20.0)	38.8 (13.6) 37.5 (20.0)	36.6 (13.3) 36.5 (19.0)	<0.0001
Social Support Score, mean (SD)	8.4 (2.8)	8.3 (2.7)	8.1 (2.5)	8.3 (2.7)	8.4 (2.6)	0.2420
Social Network Score, mean (SD)	31.8 (7.6)	32.2 (7.2)	32.2 (7.5)	32.5 (7.3)	32.1 (7.2)	0.7593
History of arthritis, n (%)	438 (54.7)	359 (49.1)	361 (50.9)	406 (52.7)	402 (55.4)	0.0888
History of cancer, n (%)	118 (14.5)	89 (12.1)	119 (16.6)	117 (15.0)	106 (14.5)	0.1956
Diabetes, n (%)	182 (22.4)	183 (24.8)	203 (28.2)	227 (29.0)	267 (36.6)	<0.0001
Hypertension, n (%) n=3773	454 (56.0)	434 (59.0)	434 (60.5)	483 (62.0)	464 (63.7)	0.1628
History of COPD, n (%)	94 (12.0)	92 (13.0)	84 (12.3)	114 (15.0)	115 (16.2)	0.0889

Table 2.6.2 Continued

History of Angina, n (%)	113 (13.9)	102 (13.8)	126 (17.5)	143 (18.3)	176 (24.1)	<0.0001
History of Congestive Heart Failure, n (%)	26 (3.2)	22 (3.0)	27 (3.8)	23 (2.9)	42 (5.8)	0.0213
History of Claudication, n (%)	10 (1.2)	12 (1.6)	11 (1.5)	24 (3.1)	37 (5.1)	<0.0001
History of MI, n (%)	60 (7.4)	47 (6.4)	63 (8.8)	79 (10.1)	109 (14.9)	<0.0001
History of stroke, n (%)	29 (3.6)	21 (2.9)	25 (3.5)	38 (4.9)	38 (5.2)	0.1025
History of TIA, n (%)	22 (2.7)	11 (1.5)	24 (3.3)	28 (3.6)	25 (3.4)	0.1011
Depression, n (%)	86 (10.6)	70(9.5)	80(11.1)	81 (10.4)	104 (14.3)	0.0429
Cognitive impairment (MMSE<27), n (%) (n=3774)	185 (22.8)	170 (23.1)	172 (24.0)	171 (21.9)	186 (25.5)	0.5354

Table 2.6.3 Ordinal regression models of the association between lifestyle factors and hospital days in the last 5 years of life

Lifestyle Factor	**Model 1*** **Odds Ratio (95% CI)**	**P value**	**Model 2**** **Odds Ratio (95% CI)**	**P value**	**Model 3** **Odds Ratio (95% CI)*****	**P value**
Alcohol		<0.0001		0.0331		0.0310
Non-drinker	Reference					
Former drinker	1.03 (0.81 - 1.32)	0.7890	1.03 (0.80 - 1.32)	0.8421	0.98 (0.76 - 1.26)	0.8560
1 to 6 drinks/week	0.76 (0.65 - 0.88)	0.0002	0.79 (0.68 - 0.92)	0.0030	0.79 (0.67 - 0.92)	0.0021
7 to 13 drinks/week	0.71 (0.54 - 0.95)	0.0188	0.84 (0.63 - 1.13)	0.2438	0.82 (0.62 - 1.10)	0.1906
≥14 drinks/week	0.77 (0.61 - 0.98)	0.0349	0.82 (0.64 - 1.06)	0.1241	0.80 (0.62 - 1.03)	0.0776
Smoking		<0.0001		0.0006		0.0124
Non-smoker	Reference					
Former Smoker	1.29 (1.12 -1.48)	0.0003	1.25 (1.08 -1.44)	0.0026	1.21 (1.04 - 1.39)	0.0107
Current Smoker	1.46 (1.19 -1.80)	0.0003	1.44 (1.16 -1.79)	0.0009	1.29 (1.04 - 1.61)	0.0207
Physical Activity (per 1000 Kcal)	1.01 (0.98 - 1.04)	0.6729	1.02 (0.99 - 1.06)	0.2078	1.02 (0.99 -1.06)	0.1589
Blocks walked per week (per 25 blocks)	0.99 (0.96 -1.02)	0.4317	1.00 (0.97 – 1.03)	0.7234	0.99 (0.96 -1.02)	0.6738

Table 2.6.3 Continued

Exercise Intensity		0.6987		0.5701		0.8190
None	Reference					
Low	1.00 (0.79 - 1.27)	0.9863	1.18 (0.92 - 1.51)	0.2019	1.19 (0.93 -1.53)	0.1637
Moderate	1.00 (0.78 - 1.29)	0.9897	1.17 (0.90 - 1.53)	0.2309	1.20 (0.92 -1.56)	0.1749
High	0.88 (0.65 - 1.20)	0.4206	1.10 (0.80 - 1.50)	0.5768	1.13 (0.82 -1.56)	0.4449
BMI		0.0027		0.0972		0.0409
<18.5	1.03 (0.63 - 1.67)	0.9219	1.09 (0.65 - 1.82)	0.7475	1.07 (0.64 - 1.78)	0.8043
(18.5, 24.99)	Reference	-	-	-	-	-
(25, 29.99)	1.14 (1.00 - 1.31)	0.0573	1.12 (0.97 - 1.29)	0.1236	1.15 (1.00 - 1.33)	0.0579
≥30	1.41 (1.18 - 1.69)	0.0002	1.27 (1.05 - 1.55)	0.0136	1.32 (1.08 - 1.60)	0.0054
Diet (AHEI)		0.9785		0.8563		0.8543
5.5-26.5	Reference					
27-34.5	0.97 (0.80 - 1.17)	0.7444	0.93 (0.77 - 1.14)	0.4918	0.94 (0.77 - 1.15)	0.5670
35-42.5	0.97 (0.80 - 1.18)	0.7550	0.96 (0.78 - 1.17)	0.6541	0.99 (0.81 - 1.22)	0.9552
43-51.5	0.93 (0.76 - 1.14)	0.5109	0.89 (0.72 - 1.10)	0.2657	0.91 (0.74 - 1.13)	0.3981
52-80.5	0.95 (0.77 - 1.18)	0.6654	0.93 (0.74 - 1.16)	0.4991	1.00 (0.80 - 1.25)	0.9885
Social Support	1.01 (0.99 -1.04)	0.3721	1.01 (0.98 -1.04)	0.5078	1.01 (0.98 -1.04)	0.5566
Social Network	1.01 (1.00 – 1.02)	0.0384	1.01 (1.00 -1.02)	0.0170	1.01 (1.00 -1.02)	0.0128

*Model 1(Core model) adjusts for socio-demographic factors and other lifestyle factors

** Model 2 adjusts for socio-demographic factors, other lifestyle factors and health factors

***Model 3 adjusts for socio-demographic factors, other lifestyle factors, health factors and age at death

3.0 CARDIOVASCULAR EVENTS, DISABILITY FREE SURVIVAL, AND OVERALL SURVIVAL

Mini E. Jacob, MD[1]; Robert Boudreau, PhD[1]; Jason L. Sanders, MD, PhD[2,3]; Alice M. Arnold, PhD[4]; Paulo Chaves, MD, PhD[5]; Janice Zgibor, PhD[1]; Steven Albert, PhD[6]; Mary Ganguli, MD[1,7], MPH; Anne B. Newman, MD, MPH[1]

[1]Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA; [2]Brigham and Women's Hospital, Boston, MA; [3]Massachusetts General Hospital, Boston, MA; [4]Department of Biostatistics, University of Washington, Seattle, WA; [5]Benjamin Leon Center for Geriatric Research and Education, Herbert Wertheim College of Medicine, Florida International University, Miami, FL; [6]Department of Behavioral and Community Health Sciences, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA; [7]Department of Psychiatry and Neurology, School of Medicine, University of Pittsburgh, Pittsburgh, PA

3.1 ABSTRACT

Background: Cardiovascular mortality rates have been falling but it is not clear whether the morbidity and disability associated with these events have reduced. It is possible that medical interventions which are preventing deaths may prolong the period of debility. In this analysis of data from the Cardiovascular Health Study, we aimed to estimate and compare the risk for disability and death associated with cardiovascular events and diagnoses in order to assess whether these events would have a greater impact on disability free survival or overall survival.

Methods: Participants free of cardiovascular disease at baseline (n=4192) were followed up for 6 years. Cardiovascular events were self-reported, confirmed from medical records and adjudicated. Mortality information was obtained during surveillance calls and death reports. Disability was assessed every six months using the Activities of Daily Living questionnaire. We used the Wei Lin Weissfeld (WLW) method was to fit marginal cox models to compare the association between cardiovascular events and disability-free survival as well as overall survival.

Results: In WLW models adjusted for confounders, incident angina was associated with shorter disability free survival (HR 1.33, P value <0.0128) and shorter overall survival (HR 1.95, P value <0.0001).The Wald test statistic examining equality of hazard ratios (p-value 0.006) indicated that the risk for shorter overall survival was greater than the risk for shorter disability-free survival. Therefore, angina was associated with a compression of the mean disabled period among participants who experienced the event, when compared to participants who did not. Similarly, MI, CHD and CHF were found to have stronger associations with a shorter survival than with a shorter disability free survival whereas for stroke, there was no significant difference between its effect on survival and disability free survival.

Conclusions: Our evidence that cardiovascular events in the population may not add a substantial burden of disability in the population is important for disability related health policy and planning. Our findings suggest that the key to disability reduction in the population may be to focus on chronic diseases which have low risk for mortality but a high risk for disability.

3.2 BACKGROUND

The age adjusted cardiovascular death rates in the US continues to fall, with 342.9 deaths per 100,000 persons reported in 2000 and 236.6 deaths per 100,000 reported in 2010.[122] Half of this decline in cardiovascular disease mortality can be attributed to primary prevention (preventive health behaviors) and half to secondary prevention (medical treatment).[123] Primary prevention delays or prevents the onset of disease and prolongs healthy life. Secondary prevention, on the other hand, despite being intended to control disease and prevent complications, can potentially expand the morbid period at the end of life by preventing death in debilitated states. In the cardiovascular disease scenario, where medical interventions are contributing substantially to prolonging life with disease, it is important to examine whether disease onset and treatment are associated with an expansion of the morbid period. It is particularly pertinent in the case of cardiovascular disease as it is a major cause of disability among older adults,[57, 124, 125] impacts a large proportion of the population and can reflect the overall morbidity experience among a large proportion of older adults in the terminal period of life.

Trends in the duration of morbidity at the end of life have been a subject of much debate over the past several decades. Fries' compression of morbidity hypothesis proposes a compression of the morbid period with increasing longevity as a result of healthy lifestyles that postpone disease[1], whereas Gruenberg's expansion of morbidity hypothesis proposes a prolongation of the morbid period due to medical interventions that prevent death.[4] Manton's theory of dynamic equilibrium suggests that the morbid period would remain stable over time.[5] Research evaluating these population aging theories has given conflicting conclusions.[40, 49, 50, 52] In this study, we propose a novel analytic method to assess the effect of cardiovascular events and their treatment on the morbid period (measured as disability) in a cohort of community

dwelling older adults participating in the Cardiovascular Health Study. We aimed to estimate and compare the hazard ratios for disability and death associated with multiple cardiovascular events and diagnoses, i.e., angina, Myocardial Infarction (MI), Coronary Heart Disease (CHD), Congestive Heart failure (CHF) and stroke, in order to assess whether these events would have a greater impact on disability free survival or overall survival. We hypothesized that if Gruenberg's morbidity expansion hypothesis was true, a cardiovascular event would reduce disability free survival to a greater extent than overall survival, thereby expanding the disabled period. In the analysis, this would be evident in the form of higher rates for the endpoint indicating the end of disability free life (incident disability or death without disability) when compared to the end-point indicating end of life (death with or without disability), in the sample population. In contrast, if the event and its treatment have a greater impact on overall survival than disability free survival, the result would be a compression of disability; this would be evident from higher rates of death associated with the event, compared to the rates for incident disability or death without disability. If the effect of the cardiovascular event on disability free survival and overall survival are the same, the event could be assumed to maintain a dynamic equilibrium of disability in the population.

3.3 METHODS

3.3.1 Study design and participants

The CHS is a population based, ongoing longitudinal multicenter study of cardiovascular disease risk in community-dwelling older adults[97]. Recruitment methods for the CHS have been previously published[98]. In brief, between June 1989 and May 1990, 5201 individuals who were 65 years old or older were recruited from a stratified random sample of Medicare recipients from four US communities: Washington County, Maryland; Pittsburgh (Allegheny County), Pennsylvania; Forsyth County, North Carolina; and Sacramento County, California. Individuals who were non-institutionalized, expected to remain in the area for 3 years, and able to give informed consent were included in the study. Individuals who were wheelchair-bound in the home or who were receiving hospice care, radiation therapy, or chemotherapy for cancer were excluded[97]. Cardiovascular disease was not an exclusion criterion for recruitment. Following the recruitment of the original cohort of predominantly Caucasian (95% Caucasian) men and women, in 1992–1993 a cohort of 687 African Americans was added. Participants completed an extensive interview and examination at the field centers at baseline. After enrollment, participants were seen annually, and were contacted by telephone at 6-month intervals until 1999. Participants provided written informed consent, and the institutional review boards at each participating center approved the study methods.

3.3.2 Cardiovascular events

CHS participants were classified at baseline according to the presence or absence of cardiovascular disease states (angina, MI, CHF, stroke) using hospital records and physician confirmation.[106, 126] Cardiovascular events were ascertained during clinic visits or surveillance telephone calls where participants were asked to provide information on all hospitalizations and outpatient diagnoses since the last contact. Participants provided authorization for release of medical information during the baseline visit. Hospital records were accessed and extracted; Medicare hospitalization data were also obtained. Hospital records were reviewed and events were adjudicated by an expert panel of CHS investigators. Details of cardiovascular event documentation and adjudication have been published.[127] For this analysis, we considered the following cardiovascular conditions – angina, MI, CHD, CHF and stroke. CHD was a composite variable which included a diagnosis of angina, MI, CHD, bypass surgery or angioplasty.

3.3.3 Disability

Disability was assessed annually using the six item self-reported difficulty with activities of daily living (ADL) questionnaire. The ADLs assessed were bathing, dressing, eating, using the toilet, walking around the home, and getting out of a bed or chair. The first report of difficulty in any of six ADLs was considered as an incident disability event.

3.3.4 Deaths

Deaths were identified at 6 month contacts and from obituaries, medical records, proxy interviews, and death certificates. Follow-up for vital status was 100% complete.

3.3.5 Potential confounders

Potential confounders were selected on the basis of their known association with cardiovascular events, disability and mortality. Age, gender, race, number of years of education, and income were self-reported at baseline. For this analysis, race was categorized as white and black. Non-black minority participants (n=18) were included with whites for the analysis. Education was categorized as ≤8 years and >8 years. Income was classified as ≤$25,000 and >$25,000. Hypertension was confirmed if self-report was accompanied by medication use or if the average seated blood pressure was ≥140/90. Diabetes was defined as fasting glucose ≥110 mg/dl or use of anti-glycemic medication. Smoking and alcohol consumption were self-reported. Participants were considered to be former alcohol drinkers if they were non-drinkers at baseline and reported 1) having stopped alcohol consumption in the past five years and/or 2) ever drank five or more drinks of any kind of alcohol almost every day. Leisure time activity (kilocalories/week) was assessed using the modified Minnesota leisure-time activities questionnaire,[99] and a weighted sum of kilocalories expended in physical activity was calculated. Standardized techniques were used to measure height and weight. The Alternate Healthy Eating Index (AHEI) was calculated from this data consistent with previous studies.[102] Body Mass Index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

3.3.6 Statistical Analysis

As the original and minority cohorts had started the study at different time points we combined their baseline data and data from follow-up years. As a result we had a total of six years of follow-up for the combined cohort. For this analysis, we excluded all participants with cardiovascular disease at baseline. Participants who reported any ADL difficulty at baseline were also excluded. Out of 5888 CHS participants, 4192 participants were free of cardiovascular disease and ADL difficulty at baseline.

We calculated the number and proportion of participants experiencing disability events and deaths in each category of baseline characteristic. We also assessed the number and proportion of participants developing disability and death among those with and without cardiovascular events during follow-up. Chi-square tests were used to compare proportions.

In survival analyses, we modeled cardiovascular events as time varying factors to leverage the extensive information on cardiovascular events and precise dates available in CHS. Time to disability was calculated as time from study onset to time of self-reported ADL difficulty in the study. Terminal missing data on disability was censored at the last observed visit. If a participant was missing disability information prior to the first report of incident disability, the mid-point of the time between the incident event and the previous observed status was used as the end-point for calculation of time to event. Participants who did not have the event were censored at the last visit. As a first step, we assessed hazard ratios for disability and death associated with each cardiovascular event using separate Cox proportional hazards models. In these models, participants who died without disability were censored at the date of death.

We used the Wei Lin Weissfeld (WLW) method[128] to fit marginal cox models to demonstrate and compare the association between the incidence of cardiovascular diagnosis and disability free survival as well as overall survival. The two major outcomes for this analysis were therefore - 1) a combined outcome which included incident disability and death without disability and 2) any death. The combined outcome indicates the end of disability free life and death indicates the end of survival. Several authors have used the WLW method to study processes with a recurring and a competing terminating event. [129, 130] In our analysis, the first occurrence of disability and death were the only events under consideration. We used the WLW model as a convenient method to test the joint hypothesis that there was no difference between those with and without cardiovascular diagnoses with respect to either endpoint. For each cardiovascular diagnosis, the WLW method generates two marginal models, one assessing hazard ratio for disability/death without disability and one estimating the hazard ratio for any death. The estimates for the effect of a cardiovascular event on these outcomes were compared using a Wald chi-square statistic. A p-value less than 0.05 was considered to be statistically significant. All analyses were performed on SAS 9.4.

3.4 RESULTS

Table 1 displays the distribution of socio-demographic factors, lifestyle factors and chronic disease according to the two main outcomes, ADL difficulty and death. There was a significantly higher proportion dying and becoming disabled among older age groups, as expected. A significantly greater proportion of women developed disability but a significantly lower proportion of women died, when compared to men. A greater proportion of blacks developed

disability but there was no difference between blacks and whites in terms of deaths. There were significantly more disability and death among participants who had a lower income (≤$25,000 per year) when compared to those with a higher annual income. A lower education (≤ 8 years) was not associated with higher rate of incident disability but the lesser educated had significantly higher proportion of deaths.

Alcohol consumption was associated with both disability and death; non-consumers were more likely to develop disability than those who consumed alcohol. With regard to death, former drinkers had the highest proportion of deaths. Smoking was not associated with disability but was associated with death. Compared to non-smokers, among whom 9.7% died, smokers had a higher proportion of deaths (16.8%). Diet, as measured by AHEI was associated with both disability and death in bivariate analysis. The lowest proportions of disability and death were among the participants in the best quintile of AHEI. Body Mass Index was associated with both disability and death. Overweight participants had the highest proportions becoming disabled but underweight participants had the highest mortality. Diabetes and hypertension were associated with both disability and death.

Table 2 describes incident disability and death among participants who ever developed cardiovascular events during follow-up as compared to those who did not. In these bivariate analyses, Angina, MI, and CHD were not associated with incident disability but were associated with death. CHF and stroke were associated with both incident disability and death.

The hazard ratios and corresponding p values from Cox proportional hazards models adjusted for confounders for disability and death outcomes are presented in Table 3. The models adjusted for age, gender, race, education income, smoking, alcohol consumption, physical activity in kilocalories (log transformed), AHEI, BMI, diabetes, and hypertension. Stroke was

the only cardiovascular event examined which was associated with significantly higher risk for disability (HR 2.53, *P* value <0.0001). All cardiovascular events were associated with a higher risk for death; the highest risk was associated with CHF (HR 3.74, P value <0.0001).

In WLW models adjusted for confounders, participants who developed incident angina during follow-up had significantly higher risk for shorter disability free survival (HR 1.33, P value <0.0128) as well as shorter overall survival (HR 1.95, P value <0.0001) compared to participants who did not develop angina. The Wald test statistic examining equality of hazard ratios had a p-value of 0.006 indicating that these hazard ratios were significantly different; the risk for shorter overall survival was greater than the risk for shorter disability free survival. Therefore, angina and its treatment were associated with a compression of the mean disabled period among participants who experienced the event, when compared to participants who did not. Similarly, MI, CHD and CHF were found to have stronger associations with a shorter survival than with a shorter disability free survival; these too were likely to compress the disabled period rather than expand it. In the case of stroke, there was no significant difference between its effect on survival and disability free survival; stroke is therefore not likely to expand or compress the average disabled period among the population experiencing the event.

3.5 DISCUSSION

We evaluated the effect of cardiovascular events/diagnoses on the disability-free survival and overall survival in a cohort of older adults over 6 years and found that Angina, MI, CHF and CHD were associated with a greater risk for shorter overall survival than shorter disability-free survival. This indicates that these events/diagnoses and their treatment are likely to be

associated with a compression of the mean disabled period in the population who experience the event, when compared to those who did not, although their average life expectancy is shorter. This further indicates that cardiovascular disease incidence in the older adult population is unlikely to contribute to the disability burden in the total population, as the population with the disease is contributing lesser years of disability compared to those who do not, by virtue of their decreased life expectancy. Stroke was found to be associated with a comparable risk for shorter survival as well as shorter disability-free survival and is therefore unlikely to have an effect on the disability burden in the total population.

Chronic diseases are the leading cause of death and disability in the US.[131] Cardiovascular disease, in particular, continues to be the leading cause of mortality[132] despite falling disease-specific death rates over the past several decades. Chronic disease related disability (limitation in usual activities) has been reported by about 13% of the US population and 46% of those older than 75.[133] Among older adults, cardiovascular disease has been implicated as an important cause of disability following arthritis and other musculoskeletal conditions.[59] Cardiovascular disease therefore, is a chronic disease which has a major double impact on older populations; a reduction in life expectancy and active life expectancy. Active life expectancy, the duration of life free of disability, is a robust measure of the duration of life free of morbidity in the population. Disentangling and comparing the effects of the disease on life expectancy and active life expectancy is crucial to understanding whether disease incidence impacts the disability burden in populations. Total, active and disabled life expectancy associated with diseases are estimated in artificial populations using life tables based on disability transition rates from longitudinal studies.[134-136] In our analysis, we have used a modeling technique used to study recurrent events in observational studies[137-140] ; it can also be

used to compare benefits to disease free survival and overall survival in clinical trials.[129, 141] To our knowledge, this is the first time that this method has been put to use to compare disability free survival and overall survival in an observational study of older adults and to test for compression versus expansion of morbidity.

Our findings provide important evidence regarding the effect of cardiovascular disease on the morbidity and mortality burden in populations. Although there has been considerable evidence regarding the decreased life expectancy associated with cardiovascular disease,[142] the relationship between cardiovascular disease and disability free survival has not been clearly elucidated. Our findings demonstrate that cardiovascular events (except MI) are associated with a reduction in disability free survival. We have also compared the effect of cardiovascular events on disability and mortality to demonstrate that cardiovascular events are associated with a compression of the disabled period in the population.

Our study has several strengths. The Cardiovascular Health Study, whose primary objective was the evaluation of cardiovascular risk factors in the older adult population, has precise documentation of cardiovascular events based on self-report, hospital records and physician adjudication. We used cardiovascular events as time-varying predictors which allowed appropriate use of available longitudinal data.[143] The Wei Lin Weissfeld model allowed us to jointly model the effect of cardiovascular events on both disability free survival and overall survival and test a joint hypothesis of no difference between the two outcomes.[129] It also calculates a robust variance estimate which allows for dependence between survival times. When compared to active life expectancy calculations using life tables, our method is simpler and amenable to routine use in observational studies of older adults.

Some limitations have to be kept in mind when evaluating the results. We measured disability in terms of self-reported ADL disability; although self-report is the most commonly used method to assess disability, it is a subjective measure. Also, disability may be a function of subclinical cardiovascular disease, disability onset could occur prior to a clinical event [144] and health could improve subsequent to the event as a result of treatment.[145] This could have attenuated associations between event and disability.

To summarize, diagnosis and treatment of cardiovascular diseases among older adults are associated more with a shorter mean survival than with a shorter disability free survival, indicating that these are unlikely to be contributing to the disability burden in populations. An aging population and the obesity epidemic is bound to result in an increasing prevalence of cardiovascular disease but our evidence suggests that current medical treatment of these conditions will not contribute to increasing disability in populations if the mortality rates due to the disease remain stable. Further decline in mortality rates may result in a change in these dynamics.

3.6 TABLES

Table 3.6.1 Baseline characteristics of 4192 CHS participants according to their disability and death outcomes during 6 years of follow-up

Characteristic	Number (%)	Participants with incident disability N (%)	P value	Participants who died N (%)	P value
Gender			<0.0001		<0.0001
Men	1663 (39.7)	357 (21.5)		289 (17.4)	
Women	2529 (60.3)	787 (31.1)		222 (8.8)	
Age group			<0.0001		<0.0001
65 - 69	1571 (37.5)	335 (21.3)		107 (6.8)	
70 - 74	1363 (32.5)	368 (27.0)		125 (9.2)	
75 - 79	785 (18.7)	232 (29.5)		131 (16.7)	
80 - 84	346 (8.3)	146 (42.0)		92 (26.4)	
84 - 89	127 (3.0)	63 (49.6)		56 (44.1)	
Race			0.0008		0.3264
Black	602 (14.4)	199 (32.9)		81 (13.4)	
White	3590 (85.6)	945 (26.3)		430 (12.0)	
Education			0.7989		<0.0001
≤8 years	590 (14.1)	164 (27.7)		116 (19.6)	
>8 years	3602 (85.9)	980 (27.2)		395 (11.0)	
Income			<0.0001		<0.0001
≤$25,000	2444 (58.3)	727(29.7)		339 (13.9)	
>$25,000	1748 (41.7)	417 (23.8)		172 (9.8)	
Smoking			0.0508		<0.0001
Never	1989 (47.5)	577 (29.0)		194 (9.7)	
Former	1678 (40.0)	429 (25.6)		229 (13.7)	
Current	525 (12.5)	138 (26.3)		88 (16.8)	

Table 3.6.1 Continued

Alcohol consumption			0.0011		<0.0001
None	1634 (39.5)	489 (30.0)		189 (11.6)	
Former	327 (7.9)	96 (29.4)		71 (21.7)	
0-6 drinks/wk	1552 (37.6)	386 (24.9)		171 (11.0)	
7-13 drinks/wk	271 (6.6)	67 (24.7)		34 (12.6)	
≥ 14 drinks/wk	349 (8.4)	86 (24.6)		42 (12.0)	
Diet (AHEI)			0.0478		<0.0001
Quintile 1	707 (19.1)	204 (28.9)		126 (17.8)	
Quintile 2	704 (19.0)	176 (25.0)		116 (16.5)	
Quintile 3	780 (21.1)	223 (28.6)		89 (11.4)	
Quintile 4	752 (20.3)	196 (26.1)		71 (9.4)	
Quintile 5	760 (20.5)	177 (23.3)		40 (5.3)	
BMI			<0.0001		<0.0001
<18.5	76 (1.8)	25 (32.9)		20 (26.3)	
(18.5, 24.99)	1598 (38.2)	380 (23.8)		215 (13.4)	
(25, 29.99)	1755 (41.9)	467 (26.6)		188 (10.7)	
≥30	756 (18.1)	271 (35.8)		86 (11.4)	
Hypertension at baseline			0.0083		<0.0001
Yes	2330 (55.7)	674 (28.9)		336(14.4)	
No	1856 (44.3)	469 (25.3)		174 (9.4)	
Diabetes at baseline			0.0093		<0.0001
Yes	1064 (25.4)	323 (30.4)		177 (16.6)	
No	3128 (74.6)	821 (26.3)		333 (10.7)	

Table 3.6.2 Occurrence of different cardiovascular events during follow-up and the distribution of incident death and disability among those with and without each event

Event	Occurrence of CVD event N (%)	Occurrence of incident disability N (%)	P value	Occurrence of death N (%)	P value
Angina			0.0923		0.0106
Yes	461 (11)	141 (30.6)		73 (15.8)	
No	3731 (89)	1003 (26.9)		437 (11.7)	
MI			0.9717		<0.0001
Yes	230 (5.5)	63 (27.4)		61 (26.5)	
No	3962 (94.5)	1081 (27.3)		449 (11.3)	
CHD			0.3563		<0.0001
Yes	539 (12.9)	156 (28.9)		146 (27.1)	
No	3653 (87.1)	988 (27.1)		364 (10.0)	
CHF			<0.0001		<0.0001
Yes	322 (7.7)	129 (40.1)		96 (29.8)	
No	3870 (92.3)	1015 (26.2)		414 (10.7)	
Stroke			<0.0001		<0.0001
Yes	243 (5.8)	114 (46.9)		80 (32.9)	
No	3949 (94.2)	1030 (26.1)		430 (10.9)	

Table 3.6.3 Results from Cox proportional hazards models testing association between cardiovascular events and disability and death during 6 years of follow-up

Cardiovascular event	HR for disability	P value	HR for death	P value
Angina	1.16	0.2959	1.92	<0.0001
MI	0.88	0.5845	2.14	<0.0001
CHD	1.15	0.3143	1.91	<0.0001
CHF	1.32	0.1340	3.79	<0.0001
Stroke	2.53	<0.0001	2.33	<0.0001

Each CVD event predictor has been adjusted for age, gender, race, education income, smoking, alcohol consumption, physical activity (log transformed kilocalories expended), AHEI, BMI, diabetes, and hypertension

Table 3.6.4 Results from WLW models comparing the hazard ratios for disability/death without disability and death for each cardiovascular disease event

Cardiovascular event	HR for disability/death without disability	P value	HR for death	P value	P value (test for equal coefficients)
Angina	1.33	0.0128	1.95	<0.0001	0.0060
MI	1.36	0.0650	2.27	<0.0001	0.0031
CHD	1.32	0.0149	1.94	<0.0001	0.0062
CHF	2.20	<0.0001	3.74	<0.0001	0.0001
Stroke	2.72	<0.0001	2.28	<0.0001	0.3848

4.0 AGE AT DEATH AND THE DURATION OF END-OF LIFE MORBIDITY

4.1 ABSTRACT

Background: A prolonged period of terminal illness is undesirable for older adults and their families; end of life care also causes considerable personal and societal expense. It is therefore important to quantify and identify factors that determine the duration of this period of terminal morbidity. We aimed to identify predictors of this period and in particular, to examine how age at death was associated with the length of this period in a population of older adults who died in the Cardiovascular Health Study (CHS).

Methods: We examined data from 3648 participants who died during follow-up in CHS. Terminal morbidity was measured as the number of continuous years of poor health experienced and reported by the participant, retrospectively, from the time of death and within the last 5 years before death. Multinomial regression models were used to examine the association between multiple socio-demographic, lifestyle and health factors and the duration of the terminal morbidity.

Results: Age at death was a strong independent predictor of the duration of end-of-life morbidity. When compared to those who died at ≤74 years, participants who died between 75 and 79 (Odds Ratio 4.8), those who died between 80 and 84 (Odds Ratio 9.7) and those who died between 8 5 and 89 (Odds ratio 14.6) had higher odds of having 3.5 to 5 years of terminal morbidity than having no years of morbidity. The odds reduced slightly to 12.1 for those who died between 90 and 94 and further to 9.6 among those who died at or after 95. Being male, being married, smoking, higher

social support, difficulty in IADL, arthritis and depression were also significant predictors of a longer terminal morbid period.

Conclusions: An increasing age at death is not associated with the duration of end-of-life morbidity in a linear fashion; morbid period is shortest for those who die in their seventies, peaks among those who die in their eighties and then shows a downward trend among deaths in the nineties. Identifying factors that promote survival to the nineties would help delineate factors associated with a compressed period of morbidity. Smoking cessation, arthritis management and treatment of depression could be important interventions for improving health at the end of life.

4.2 BACKGROUND

A majority of Americans die by their early eighties due to fatal illnesses like cardiovascular disease, cancer, chronic lower respiratory disease or stroke.[146] Terminal prolonged illness is undesirable for individuals and their families[147, 148] ; end-of-life care also inflicts considerable personal and societal expense. [149, 150] Therefore, reducing morbidity at the end of life is an important objective for clinicians and researchers involved in geriatric care. Medical advances in disease management are focused on obtaining this goal but by extending the life span may in fact be achieving the opposite of what is intended. In this context, quantification and evaluation of this terminal period of poor health assumes immense importance. Unfortunately, research on this has been limited by the dearth of observed data on this period; very few cohorts of older adults have been followed until extinction with adequate measurement of their terminal morbid period.

The effect of longevity on the length of the morbid period at the end of life has been a source of debate among gerontologists over the past several decades. Early on, when the increasing

life expectancy among older adults became evident, multiple theories were proposed to describe the relationship of this increasing longevity on the morbid period. The compression of morbidity hypothesis proposed that increasing longevity would be associated with a reduction in the duration of morbidity at the end of life.[1] On the other hand, the expansion of morbidity hypothesis indicated that the additional years of life gained would be years of poor health.[4] A majority of the literature evaluating these contradicting hypotheses has focused on population level changes over time, thereby examining the presence of a compression or expansion as life expectancy increases.[40, 49] To a limited extent, observational studies of centenarians have tested whether these exceptional survivors are relatively healthier when compared to those who don't survive as long, albeit with contradicting results.[12, 52] There is a lack of information regarding the association between increasing survival and morbidity at the end of life in community based samples which are more representative of the general population. It has been proposed, but not proven, that among those who do not have the potential for exceptional longevity, compression and expansion may co-exist depending on the age of the cohort being examined.[151]

The Cardiovascular Health Study (CHS), a cohort of older adults, currently in its 27th year of follow-up, provides a unique opportunity to examine the end-of-life morbid period. About 80% of the original participants have died over the years at different ages spanning from 66 to 108, leaving behind a wealth of data on morbidity and disability at the end of life. In this study, we aimed to quantify the duration of a contiguous period of poor self-reported health at the end of life among the decedents and to examine potential predictors of this period, particularly the age at death. Examining the relationship between the age and death and the morbid period would provide information on whether greater survival was associated with a compression or expansion of the morbid period in a representative population. We hypothesized that a higher age at death would

be associated with a greater duration of the morbid period as indicated by the expansion of morbidity hypothesis.

4.3 METHODS

4.3.1 Study design and participants

The CHS is a community based longitudinal study of risk factors for the development of cardiovascular disease among older adults. Between May 1989 and June 1990, 5201 participants were enrolled; a supplemental cohort of 687 African Americans was added in 1992-1993. Eligible individuals were identified from a random sample of the Medicare eligibility rosters in four U.S. communities: Washington County, Maryland; Pittsburgh (Allegheny County), Pennsylvania; Sacramento County, California; and Forsyth County, North Carolina. Eligible individuals had to be non-institutionalized, expecting to remain in the area for the following 3 years, not under active treatment for cancer, not wheelchair bound and not requiring a proxy respondent at recruitment. Household members of the sampled individual were recruited, if eligible. The institutional review boards of all four sites and the coordinating center at the University of Washington in Seattle approved the study. All participants gave informed consent. Participants completed an extensive interview and examination at the field centers at baseline. After enrollment, participants were seen annually, and were contacted by telephone at 6-month intervals until 1999. Since 1999, participants have been contacted every 6 months by telephone to ascertain health status including general health, cardiovascular events, hospitalizations, disability and deaths.

For the purpose of this analysis, we identified participants who reported good health at recruitment (n=4380) and from these, selected all participants who had died by the end of follow-up (December 30th, 2012), the latest date for which adjudicated death status is available in CHS. The final sample size was 3648.

4.3.2 Terminal morbidity

In this study, 'terminal morbidity' was measured as the number of continuous years of poor health experienced and reported by the participant, retrospectively, from the time of death and within the last 5 years before death. Participants reported their general health status every 6 months, during clinic visits or during telephone interviews. We therefore examined reports of general health at 1 to 44 time points starting from baseline (1989 -1990) to the end of follow-up (2012). The response to the question "Would you say, in general, your health is excellent, very good, good, fair or poor?" was dichotomized; participants who reported excellent, very good and good health were categorized as having good health and those who reported fair and poor health were categorized as having poor health. Self-reported health status was not available for any participant at 3 time points (study years 4, 23 and 23.5). Among the remaining years for which health status was available, 3 to 21% of participants were missing data at any time point. All missing values for self-reported health were imputed using linear interpolation as described below.

4.3.3 Linear interpolation of missing data

Linear interpolation was performed on all observations with baseline value of self-reported health in CHS (n=5875); 13 participants missing baseline value were excluded. All observed data on self-reported health were recoded to excellent = 95; very good = 90; good = 80; fair = 30; poor = 15; dead = 0, values determined by the probability of being in excellent, very good, or good health ("healthy") one year later.[152] Death status was incorporated into the measure as analyzing self-reported health without inclusion of death has been shown to be too optimistic.[153] Missing data were imputed by linear interpolation of the participant's own data over time and rounded back to the original scale.[154] Terminal missing data on participants who were alive at the end of follow-up were imputed by carrying forward the last value. Note that these observations were not used for this analysis. Linear interpolation has been demonstrated as the best method for imputing health status in longitudinal studies.[155] A sensitivity analysis done to examine the effect of imputation is described in the analysis section.

4.3.4 Identification of deaths

Deaths were identified at 6 month contacts and from medical records, obituaries, proxy interviews, and death certificates. Follow-up for vital status was 100% complete.

4.3.5 Predictors

Gender, race, number of years of education, income, and marital status were self-reported at baseline. For this analysis, race was categorized as white and black. Non-black minority

participants (n=18) were included with whites for the analysis. Education was categorized as ≤8 years and >8 years. Income was classified as ≤$25,000 and >$25,000. Age at death was calculated from the birth date and the date of death.

Lifestyle factors were assessed at baseline. Smoking and alcohol consumption were self-reported. Participants were considered to be former alcohol drinkers if they were non-drinkers at baseline and reported 1) having stopped alcohol consumption in the past five years and/or 2) ever drank five or more drinks of any kind of alcohol almost every day. Leisure time activity (kilocalories/week) was assessed using the modified Minnesota leisure-time activities questionnaire[99], and a weighted sum of kilocalories expended in physical activity was calculated. The highest intensity of reported physical activity was categorized as the exercise intensity of participants (high, moderate, low or none).[100] Distances walked were assessed by self-report of blocks walked in the previous week. Dietary habits were assessed for the original cohort alone using the picture-sort National Cancer Institute food frequency questionnaire.[101] The Alternate Healthy Eating Index (AHEI) was calculated from this data consistent with previous studies.[102] Standardized techniques were used to measure height and weight. Body Mass Index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Social support was measured using a six-item version of the Interpersonal Support Evaluation List,[103] and social networks (size, closeness and frequency of contacts) were measured using the 10-item Lubben social network scale. [104]

Health status was characterized using multiple variables. Activities of Daily Living (ADL) were self-reported in six domains (eating, bathing, toileting, dressing, getting out of bed or chair, and walking around the home); Instrumental Activities of Daily Living (IADL) were also self-reported in six domains (telephone use, shopping, preparing food, performing light

household work, performing heavy household work, and managing finances). Participants were categorized as having or not having any difficulty in any of the domains of ADL (ADL difficulty) and IADL (IADL difficulty). Health was self-reported and participants were categorized as those reporting poor health and those reporting better than poor health. Cognition was measured using the Mini Mental Status Examination[105] and categorized as severe cognitive impairment (0 - 17), moderate impairment (18-23), mild impairment (24-26) and normal (>27). Hypertension was confirmed if self-report was accompanied by medication use or if the average seated blood pressure was ≥140/90. Diabetes was defined as fasting glucose ≥110 mg/dl or use of anti-glycemic medication. Angina, myocardial infarction, heart failure, peripheral artery disease, stroke, and transient ischemic attack were identified using self-report and hospitalization records.[106] COPD was defined as self-reported asthma, bronchitis or emphysema. Depression was assessed using the 10-item version of the Center for Epidemiologic Studies Depression Scale and participants were categorized as depressed (≥ 10) or not depressed (<10).[107] All confounders were assessed at baseline. Missing values for co-variates were imputed as described previously.[108]

4.3.6 Statistical analysis

To estimate terminal morbidity, we retrospectively examined the half-yearly reports of general health from the date of death to five years from death. The morbid years were counted backwards as the number of years of poor health contiguously reported, starting from the visit prior to death. If the participant reported good health at the time point prior death, these were identified as participants without a terminal morbid period. Participants who reported more than

5 years of a contiguous period of poor health are categorized as having had 5 years of poor health before death.

All statistical analyses were performed with SAS software, version 9.4 (SAS Institute, Inc., NC). We examined the distribution, mean duration and range of the morbid period in the population. Due to the skewed nature of the distribution of the morbid period we categorized the morbid period into 0, 0.5 -1, 1.5 to 3, and 3.5 to 5 years. Bi-variate associations between the potential predictors and the categories of the morbid period were examined using chi-square tests and non-parametric Kruskal Wallis tests. We used a manual backwards elimination process to generate a final multinomial regression model predicting the terminal period of morbidity, as recommended by Sun et al.[156] An initial model was run with all the predictors. Subsequently, the variable with the largest p-value was removed and the model was run with the remaining predictors. This process was repeated until all the variables in the model were statistically significant.

We performed a sensitivity analysis including only participants who had less than 5% of their measurements missing over time. This sample was used to test the findings of the final model obtained from the backwards elimination process and assess the effects of the imputation on the results.

4.4 RESULTS

Table 4.6.1 and Figure 4.6.1 demonstrate the distribution of the terminal years of poor health among the 3648 participants in the study. Among those who died at or before 74, 75.6% died without any reported terminal morbidity or only half a year of poor health prior to death. This

percentage was less among those who died between 75 and 79 (61%) and decreased further with increase in age at death. Among those who died between 80 and 84, 47.9% had this minimal morbidity pattern while 45.5% of those who died between 85 and 89 had this experience. Among those who died between 90 and 94, there was a reversal in the trend and this group had an increase in the proportion of participants experiencing less than 6 months of poor health (49.2%). This proportion increased further in the group dying after 95 (54%).

A graphical examination of the distribution of the terminal years of poor health, using smoothing Loess plots (Graph 4.6.2) revealed that the mean duration of the morbid period increased initially and then plateaued and then showed a slight downward trend with increasing age at death. An examination of the descriptive statistics of this period according to age at death revealed the same trend (Table 4.6.2).

Table 4.6.3 describes the baseline characteristics of the study population according to the length of the terminal morbidity. Gender, race, age at death, smoking, physical activity, blocks walked, maximal intensity of exercise, social support, difficulty in IADL, arthritis and depression were found to be significantly associated with the number of terminal years of poor health. Men were more likely to have lesser period of terminal morbidity than women. Black participants, those with poor social support, depression and arthritis tended to have longer periods of terminal morbidity while greater physical activity, exercise intensity and more walking seemed to be associated with a lesser morbid period. Age at death was significantly associated with the morbid period and exhibited a non-linear relationship. Participants at the ends of the spectrum of survival, i.e., those who were survived the shortest and those who lived the longest, were more likely to have a shorter morbid period compared to the middle groups.

Results from the final parsimonious model predicting the terminal morbid period are displayed in Table 4.6.4. Age at death, gender, marital status, smoking, social support, difficulty in IADL, arthritis and depression were significant predictors of the terminal morbid period in the final model. Age at death was a strong independent predictor of the duration of the morbid period. The highest risk differences were found between having 0 years of morbidity and 3.5 to 5 years of morbidity. When compared to those who died at ≤74 years, participants who died between 75 and 79 had a 4.8 time higher odds of having 3.5 to 5 years of terminal morbidity than having no years of morbidity (p=0.01). The odds increased to 9.7 times for those who died between 80 and 84 (p-value 0.0002), and further to 14.6 for those who died between 85 and 89 (p-value <0.0001). The odds reduced slightly to 12.1 for those who died between 90 and 94 (p-value <0.0001) and further to 9.6 among those who died at or after 95 (p-value 0.0002).

Men, when compared to women, had about 30% reduced odds of having 1.5-3 years or 3.5-5 years of morbidity than having none. Married participants had 30% higher odds of having a 3.5 -5 year morbid period than no morbid period when compared to those who were not married at baseline. Both former and current smokers had higher odds of being in a longer morbid period when compared to non-smokers. Those who had depression at baseline had higher odds for reporting a greater morbid period at the end of life, when compared to those who did not have depression. A higher social support score, indicative of a lower social support was associated with lower odds of having 0.5 to 1 years of poor health compared to none.

Odd ratios and confidence intervals obtained from a sensitivity analysis including 2168 participants with less than 5% missing values are presented in Table 4.6.5. The odds ratios were attenuated to an extent but remained substantial with the direction and pattern of the relationship remaining the same.

4.5 DISCUSSION

We analyzed data from 3648 decedents in CHS and found that age at a death had a non-linear association with the duration of poor health at the end of life. Participants who died between 85 and 89 had the highest risk for a longer period of poor health when compared to those with a shorter or longer life expectancy. Other significant factors that increased the risk of a longer terminal period of poor health were being male, being black, being married, or having arthritis, IADL difficulty or depression at baseline.

Self-reported health is a valid and reliable measure of health status and is highly correlated with disease[26, 157], physical function[158, 159] and mortality.[160-162] It has also been shown to predict mortality above and beyond objective measures of health.[24, 163] Self-reported health has been used previously in CHS to define years of healthy life, which has properties similar to disability free life expectancy.[30, 164] We have therefore used this measure to quantify and model the terminal period of poor health among CHS participants.

Our study highlights the strong relationship between age at death and the duration of terminal morbidity in individuals. Most of the literature which has evaluated this phenomenon has studied this relationship among centenarians. Exceptional longevity has been associated with a reduced burden of disease and disability in some studies of centenarians[52, 165] but some reports indicate that this may not be true.[8, 166] Heterogeneity in health and functioning may be the most plausible characterization of centenarians[12] but patterns among the more average-lived are still unclear. Our study examines a more representative population and allows for examining the relationship over a wide age range.

There could be different factors influencing the trend that we observed in the relationship between survival and the terminal morbid period. It is possible that compression starts appearing only when life expectancy nears the maximal life expectancy. The preventive factors that contribute to survival greater than 90 may be adequate to cause compression whereas factors responsible for extending the life span to the eighties may favor expansion. The curvilinear trend in the morbid period with age may reflect the pattern seen in incidence of chronic diseases with age among older adults.[167] The incidence of many fatal chronic diseases which peak in early old age start declining among the oldest old. Thus the oldest old may have lesser disease and less reports of poor health at the end of life. Those who die after 85 have been shown to have a frailty index similar to those who died before 75, despite the 10 year difference in survival, again pointing to a comparatively better health among those who survive to 85 or later.[168]

Our analysis does not directly address the compression/expansion of morbidity hypotheses, which pertain to a population level change in the duration of the morbid period over time as a result of an increasing trend in life expectancy. We have evaluated it with a different perspective, and have tested whether compression/expansion of the morbid period is true for individuals who live longer than others in the same cohort. This is a parallel epidemiologic question that can support the broader demographic question of compression versus expansion in the population. If compression or expansion is true at the individual level, there is considerable probability that population level changes will reflect individual level effects.

Gender differences in morbidity and disability in old age are well known.[169, 170] Although there might be gender differences in how men and women report their health in younger ages, older men and women tend to report poor health equally, even though women have worse health.[171] Therefore a reporting bias is more likely to have attenuated the effect of gender. It is

well known that blacks experience a greater burden of morbidity and disability[172]; our findings confirm that disparity exists in the relative duration of the morbid period as well. A higher social support and being married are likely to be contributing to longer morbidity by providing the support required to prolong life in a debilitated state. Smoking is a powerful risk factor that predicts health and mortality[173]; we have demonstrated its effect on the duration of the end-of-life morbidity as well, in our analysis. Depression has been shown to affect the self-report of health[174] and also increase the risk for chronic disease.[175] The effect seen may be a combination of the change to the affect influencing the self-report as well as more objective change in health.

Our study has several strengths. We had a large sample of older adults who died while being observed in a community based cohort study with systematic measures of health and morbidity. Self-rated health was reported consistently throughout the study providing a total of 23 years of follow-up. The CHS study population is well characterized, and provided a comprehensive measure of socio-demographic, lifestyle and health factors to develop a predictive model for poor health at the end of life. Mortality follow-up was 100% complete and dates of death were accurately identified. Certain limitations have to be kept in mind when considering the results. The subjectivity of self-rated health has to be considered; there could be a mis-match between subjective perceptions and objectively measured health status, especially among the oldest old.[176] Lifestyle and health factors were measured at baseline. Deaths of participants have occurred at a wide range of years from baseline during which diseases could have been accumulated at different rates and lifestyle changes could have occurred. The effect of the age at death therefore is not unadjusted for the excess burden of disease and lifestyle changes accumulated between baseline and the beginning of the morbidity measurement (5 years before death). Participants who lived longest were also in the study for the longest time and therefore

could have accumulated more disease than those who died close to the study baseline. If available, updated measures could potentially attenuate the effect of age at death to some extent and also affect coefficients for the different age at death categories differently.

In conclusion, an increasing age at death is not associated with the duration of end-of-life morbidity in a linear fashion; morbid period peaks among those who die in their eighties and then shows a downward trend among deaths in the nineties. Identifying factors that promote survival to the nineties would help delineate factors associated with a compressed period of morbidity. Smoking cessation, arthritis management and treatment of depression could be important interventions for improving health at the end of life.

4.6 TABLES

Table 4.6.1 Distribution of 3648 CHS participants according to age at death and terminal morbidity

Age at Death	Number of years of poor health at the end of life											
	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	Total
<=74	56 (37.8)	56 (37.8)	12 (8.1)	11 (7.4)	6 (4.1)	1 (0.7)	3 (2.0)	0 (0.0)	1 (0.7)	1 (0.7)	1 (0.7)	148
75-79	144 (35.6)	103 (25.4)	45 (11.1)	29 (7.2)	16 (4.0)	16 (4.0)	14 (3.5)	11 (2.7)	5 (1.2)	4 (1.0)	18 (4.4)	405
80-84	210 (27.1)	161 (20.8)	119 (15.3)	65 (8.4)	55 (7.1)	35 (4.5)	26 (3.4)	25 (3.2)	14 (1.8)	19 (2.5)	47 (6.1)	776
85-89	280 (25.5)	221 (20.1)	151 (13.7)	86 (7.8)	82 (7.5)	52 (4.7)	33 (3.0)	32 (2.9)	20 (1.8)	35 (3.2)	108 (9.8)	1100
90-94	258 (30.4)	160 (18.8)	99 (11.7)	71 (8.4)	61 (7.2)	30 (3.5)	26 (3.1)	31 (3.7)	15 (1.8)	14 (1.7)	85 (10.0)	850

Table 4.6.1 Continued

>=95	139 (36.9)	62 (17.1)	41 (11.7)	26 (6.5)	22 (6.5)	7 (1.9)	12 (3.3)	15 (4.1)	7 (1.9)	4 (1.1)	34 (9.2)	369
Total	1087	763	467	288	242	141	114	114	62	77	293	3648

Table 4.6.2 Mean duration of terminal morbidity among 3648 CHS participants with different ages at death

Age at Death	N	Mean(SD)	Q1 (Median) Q3	Range
<=74	148	0.6 (0.9)	0 (0.5) 0.5	0 - 5
75-79	405	1.0 (1.4)	0 (0.5) 1.5	0 - 5
80-84	776	1.3 (1.5)	0 (1.0) 2.0	0 - 5
85-89	1100	1.5 (1.6)	0 (1.0) 2.5	0 - 5
90-94	850	1.4 (1.6)	0 (1.0) 2.0	0 - 5
>=95	369	1.3 (1.6)	0 (0.5) 2.0	0 - 5

Table 4.6.3 Baseline characteristics of 3648 CHS participants according to duration of terminal morbidity in the last 5 years

	Total	**0 years**	**0.5-1 years**	**1.5-3 years**	**3.5-5 years**	**P value**
n		1087	1230	785	546	
Men, n (%)	1686 (46.2)	534 (49.1)	593 (48.2)	335 (42.7)	224 (41.0)	0.0002
Black, n (%)	405 (11.1)	106 (9.8)	133 (10.9)	93(11.9)	73 (13.4)	0.0227
Age at death						0.0001
<=74	148 (4.1)	56 (5.2)	68 (5.5)	21 (2.7)	3 (0.6)	
75-79	405 (11.1)	144 (13.3)	148 (12.0)	75 (9.6)	38 (7.0)	
80-84	776 (21.3)	210 (19.3)	280 (22.8)	181 (23.1)	105 (19.2)	
85-89	1100 (30.2)	280 (25.8)	372 (30.2)	253 (32.2)	195 (35.7)	
90-94	850 (23.3)	258 (23.7)	259 (21.1)	188 (24.0)	145 (26.6)	
>=95	369 (10.1)	139 (12.8)	103 (8.4)	67 (8.5)	60 (11.0)	
Education ≤8 years, n (%)	456 (12.5)	134 (12.3)	162 (13.2)	90 (11.5)	70 (12.8)	0.8939
Income≤$25,000, n (%)	2111(57.9)	601 (55.3)	725 (58.9)	461 (58.7)	324 (59.3)	0.0985
Married, n (%)	2449 (67.1)	726 (66.8)	806 (65.5)	539 (68.7)	378 (69.2)	0.1868

Table 4.6.3 Continued

Any ADL difficulty at baseline, n (%)	169 (4.6)	41 (3.8)	59 (4.8)	39 (5.0)	30 (5.5)	0.1024
Any IADL difficulty, n (%)	709 (19.4)	175 (16.1)	266 (21.6)	154 (19.6)	114 (20.9)	0.0302
Smoking, n (%)						0.0007
Never-smoker	1639 (44.9)	546 (50.2)	514 (41.8)	338 (43.1)	241 (44.1)	
Former smoker	1577 (43.2)	426 (39.2)	580 (47.2)	356 (45.4)	215 (39.4)	
Current smoker	432 (11.8)	115 (10.6)	136 (11.1)	91 (11.6)	90 (16.5)	
Alcohol consumption, n (%)						0.4618
Non-drinker	1362 (37.8)	406 (37.9)	457 (37.5)	293 (37.8)	206 (38.3)	
Former drinker	289 (8.0)	85 (7.9)	94 (7.7)	62 (8.0)	48 (8.9)	
1-6 drinks/week	1395 (38.7)	413 (38.5)	466 (38.3)	310 (40.0)	206 (38.3)	
7-13 drinks/week	239 (6.6)	75 (7.0)	77 (6.3)	51 (6.6)	36 (6.7)	
>=14 drinks/week	319 (8.9)	93 (8.7)	124 (10.2)	60 (7.7)	42 (7.8)	
BMI, n (%)						0.1352
<18.5	54 (1.5)	13 (1.2)	22 (1.8)	10 (1.3)	9 (1.7)	
18.5 -24.99	1409 (38.8)	432 (40.0)	475 (38.7)	297 (38.0)	205 (37.6)	
25.00 - 29.99	1523 (41.9)	456 (42.2)	510 (41.6)	342 (43.8)	215 (39.4)	

Table 4.6.3 Continued

>=30	649 (17.9)	180 (16.7)	220 (17.9)	132 (16.9)	117 (21.4)	
Physical Activity in Kcals, mean (SD)	1829.7	1870.1	1867.6	1880.2	1591.0	0.0214
Blocks walked last week, mean (SD)	42.5 (56.5)	43.8 (57.5)	45.5 (58.7)	41.0 (57.6)	34.8 (46.5)	0.0011
Moderate or high exercise intensity, n (%)	1685 (46.2)	533 (49.0)	565 (45.9)	344 (43.8)	243 (44.5)	0.0289
Alternate Healthy Eating Index, mean (SD)	39.7 (13.4)	39.7 (13.5)	39.4 (13.6)	40.8 (13.2)	39.1 (13.3)	0.0883
Social Support Score, mean (SD)	8.2 (2.6)	8.2 (2.6)	8.0 (2.4)	8.3 (2.6)	8.5 (2.7)	0.0027
Social Network Score, mean (SD)	32.6 (7.3)	32.6 (7.4)	32.6 (7.3)	32.6 (7.0)	32.5 (7.5)	0.9661
History of arthritis, n (%)	1721 (47.7)	463 (43.2)	576 (47.2)	414 (53.6)	268 (49.7)	0.0002
History of cancer, n (%)	521 (14.3)	147 (13.6)	186 (15.2)	110 (14.0)	78 (14.3)	0.7848
Diabetes, n (%)	525 (14.4)	154 (14.2)	188 (15.3)	109 (13.9)	74 (13.6)	0.6251
Hypertension, n (%)	2113 (58.0)	635 (58.5)	714 (58.3)	459 (58.5)	305 (55.9)	0.4179
History of COPD, n (%)	393 (11.1)	109 (10.3)	134 (11.2)	90 (11.9)	60 (11.3)	0.3860
History of CHD, n (%)	602 (16.5)	168 (15.5)	212 (17.2)	126 (16.1)	96 (17.6)	0.3962
History of Congestive Heart Failure, n (%)	92 (2.5)	30 (2.8)	35 (2.9)	15 (1.9)	12 (2.2)	0.2637
History of Claudication, n (%)	66 (1.8)	15 (1.4)	25 (2.0)	13 (1.7)	13 (2.4)	0.2427
History of stroke, n (%)	120 (3.3)	38 (3.5)	44 (3.6)	23 (2.9)	15 (2.8)	0.3231

Table 4.6.3 Continued

Depression (CESD >10), n (%)	268 (7.4)	54 (5.0)	99 (8.1)	56 (7.1)	59 (10.8)	0.0001
Cognitive impairment (MMSE<27), n (%) (n=3774)	746 (20.5)	220 (20.3)	240 (19.5)	172 (22.0)	114 (20.9)	0.4734

Table 4.6.4 Final multivariate multinomial regression model predicting duration of terminal morbidity among 3648 CHS participants

Characteristic	**0.5-1 year versus 0 years**	**P value**	**1.5-3 years versus 0 years**	**P value**	**3.5-5 years versus 0 years**	**P value**
Age at death						
<=74	Reference					
75-79	0.85 (0.56 - 1.31)	0.4644	1.33 (0.75 - 2.38)	0.3326	4.81 (1.42 - 16.30)	0.0116
80-84	1.13 (0.75 - 1.69)	0.5552	2.28 (1.32 - 3.93)	0.0031	9.72 (2.96 - 31.90)	0.0002
85-89	1.13 (0.76 - 1.68)	0.5440	2.37 (1.38 - 4.06)	0.0017	14.56 (4.48 - 47.56)	<0.0001
90-94	0.86 (0.58 - 1.29)	0.4783	1.95 (1.13 - 3.36)	0.0166	12.08 (3.69 - 39.54)	<0.0001
>=95	0.65 (0.41 - 1.01)	0.0576	1.29 (0.71 - 2.34)	0.3972	9.58 (2.86 - 32.08)	0.0002
Male Gender	0.94 (0.78 - 1.13)	0.4997	0.69 (0.56 - 0.85)	0.0005	0.71 (0.56 - 0.89)	0.0033
Married status	0.92 (0.76 - 1.11)	0.3579	1.20 (0.97 - 1.48)	0.0989	1.32 (1.04 - 1.68)	0.0226
Smoking						
Non-smoker	Reference					
Former Smoker	1.48 (1.23 - 1.78)	<0.0001	1.49 (1.21 - 1.83)	0.0002	1.35 (1.06 - 1.71)	0.0133
Current Smoker	1.27 (0.95 - 1.69)	0.1059	1.37 (1.00 - 1.90)	0.0530	2.32 (1.66 - 3.24)	<0.0001
Social support score	0.96 (0.93 - 1.00)	0.0228	1.02 (0.99 - 1.06)	0.2459	1.03 (0.99 - 1.08)	0.1209
Any IADL difficulty	1.39 (1.11 - 1.73)	0.0036	1.13 (0.88 - 1.45)	0.3563	1.21 (0.92 - 1.60)	0.1743
Arthritis	1.11 (0.93 - 1.31)	0.2409	1.43 (1.18 - 1.73)	0.0003	1.19 (0.96 - 1.47)	0.1164
Depression	1.73 (1.21 - 2.48)	0.0026	1.42 (0.95 - 2.12)	0.0902	2.18 (1.45 - 3.27)	0.0002

Table 4.6.5 Results from a sensitivity analysis of the final model including 2168 participants with less than 5% missingness

Characteristic	1 year versus 0 years	P value	2-3 years versus 0 years	P value	4-5 years versus 0 years	P value
Age at death						
<=74	Reference					
75-79	0.91 (0.58 - 1.43)	0.6867	1.57 (0.78 - 3.12)	0.2038	3.04 (1.47 - 16.89)	0.0839
80-84	1.12 (0.73 - 1.73)	0.5972	2.55 (1.32 - 4.92)	0.0054	5.15 (1.52 - 17.50)	0.0086
85-89	1.21 (0.79 - 1.85)	0.3914	3.09 (1.61 - 5.93)	0.0007	7.83 (2.33 - 26.35)	0.0009
90-94	1.09 (0.69 - 1.71)	0.7227	2.23 (1.12 - 4.41)	0.0220	9.22 (2.70 - 31.49)	0.0004
>=95	0.74 (0.44 - 1.26)	0.2678	1.24 (0.56 - 2.73)	0.5950	6.56 (1.80 - 23.86)	0.0043

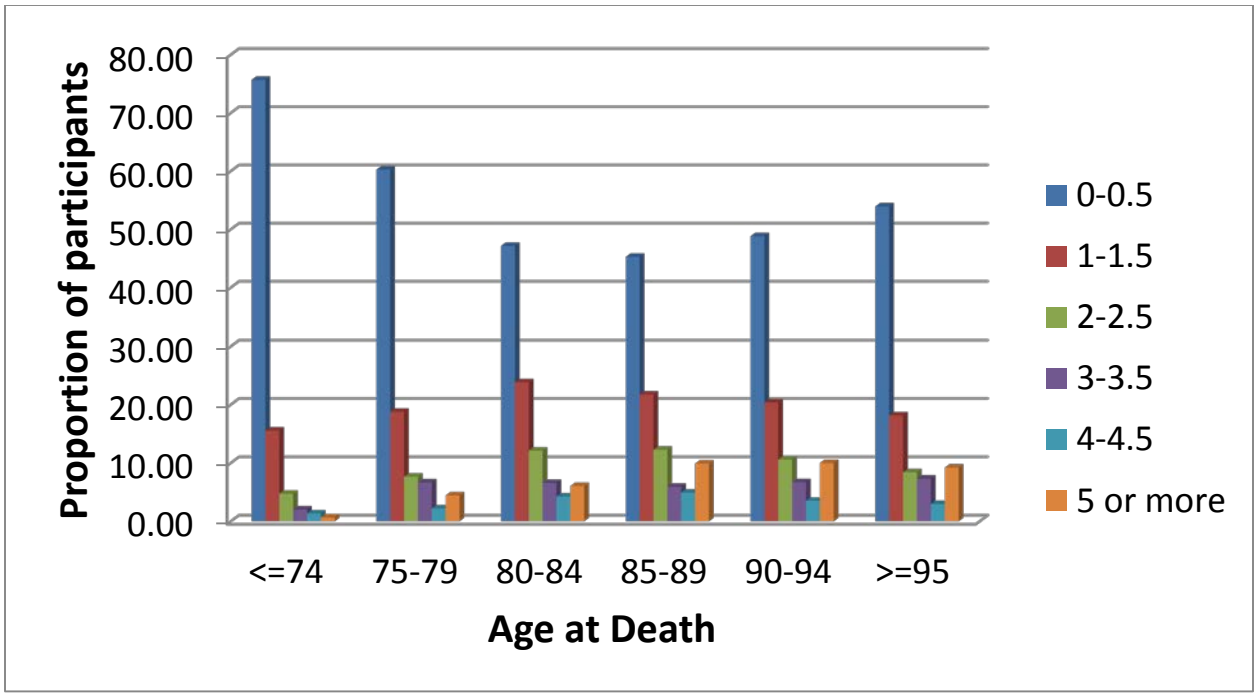

Figure 4.6.1 Distribution of participants according to age at death and duration of end-of-life morbidity

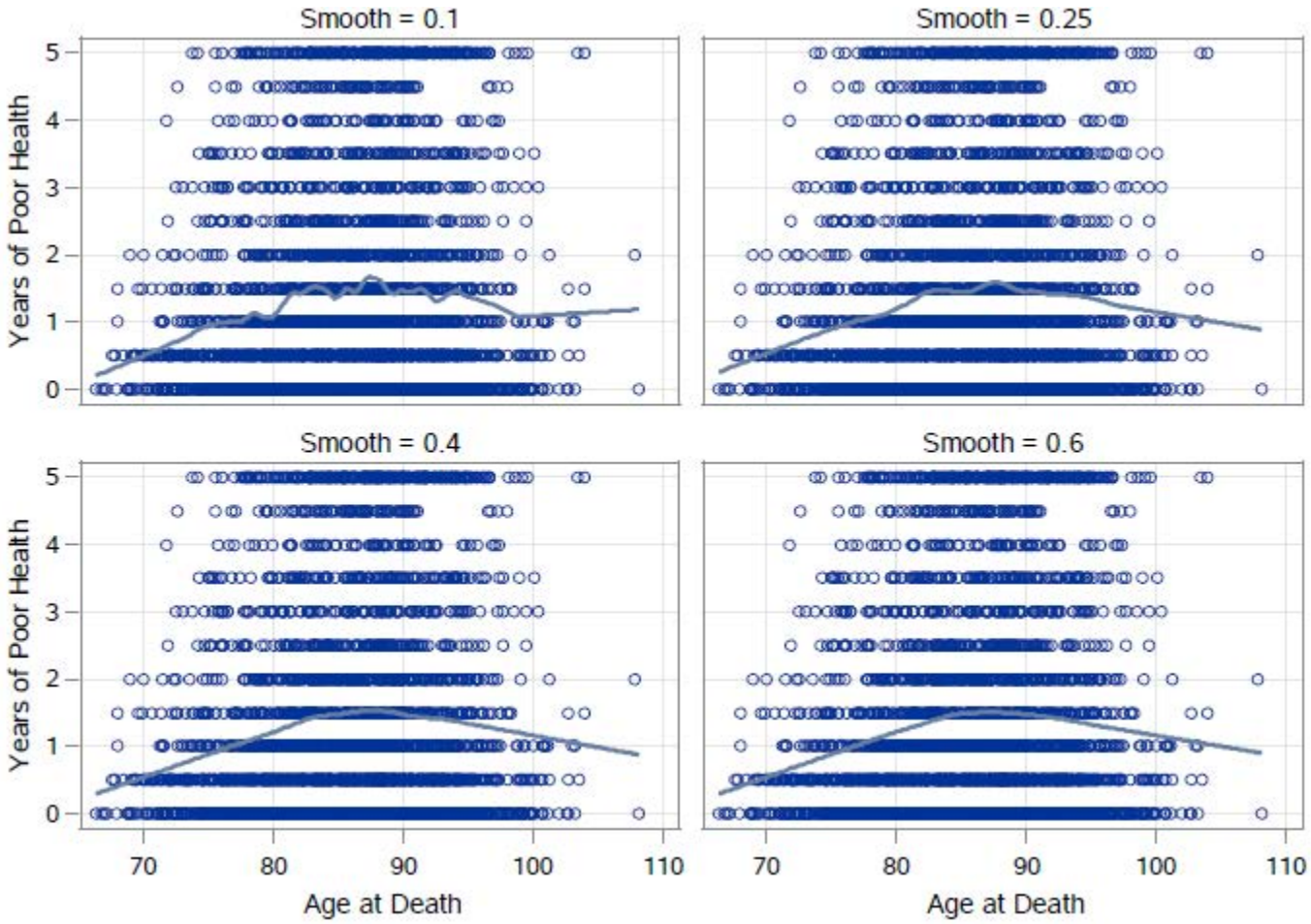

Figure 4.6.2 Smoothing Loess plots demonstrating relationship between age at death and the number of years of poor health in the last 5 years of life

5.0 SUMMARY AND PUBLIC HEALTH SIGNIFICANCE

The world's population is aging at a rapid rate. Even in developing countries, death rates are falling and more and more people live to enter old age. In terms of sheer numbers, the older adult population in developing countries, particularly China and India, are staggering. Along with aging of the population, these countries are experiencing the phenomenon of epidemiologic transition. Infectious diseases are being replaced by chronic degenerative diseases especially cancers and cardiovascular disease, which health systems are not adequately prepared to deal with, especially in large numbers. In developed nations, where chronic diseases have been the main cause of death for several decades now, the aging of the population still causes concern in terms of increasing financial costs and strain on resources.

It was in the context of this increasing life expectancy and the potential for increased burden of chronic diseases that the population aging theories were proposed, all pertaining to the duration of the morbid period at the end of life. The duration of the morbid period is of great significance because this will decide the total morbidity burden in the population and thereby health care costs to the nation. But in the rush to identify the population level changes over time and answer the question of whether there is compression or not, the epidemiologic basis of these aging theories were not adequately tested. For example, although the compression of morbidity theory proposed that healthy lifestyle factors would compress the morbid period, there is hardly any research which directly tests the effect of lifestyle factors on the observed morbid period in individuals. It was also not understood as to what diseases would extend the morbid period and what would not. This is very crucial to make sure that prevention efforts meant to reduce the morbidity burden are directed at the right diseases. The most basic question of whether increasing

age at death is associated with a linear increase or decrease in the population was also left unanswered. It was with the objective of answering these pertinent epidemiologic questions that this dissertation was executed.

The first project evaluated the effect of lifestyle factors on hospital days at the end of life, and found that certain late-life lifestyle factors could continue to impact end-of-life hospital days. However in general, much of their effect was attenuated by health related factors. This result contains an important public health policy message. Although some lifestyle changes like smoking cessation and weight control among the obese may reduce hospital stay, this outcome is mostly a function of an individual's disease burden. To reduce the escalating hospital costs incurred by an aging population, the focus should be on the prevention and control of chronic disease. Lifestyle interventions among older adults may not be a very effective strategy at this point because unhealthy lifestyles, if any, have already had their effect by way of inducing disease.

The second project evaluated the effect of cardiovascular diseases on the disability burden in the population. Findings revealed that cardiovascular diseases do not increase the disability burden in the population thereby indicating that cardiovascular diseases may not be the priority disease to control in order to reduce the disability burden in the aging population. The focus should be on diseases with lower mortality but higher disability rates.

The third project evaluated the effect of age at death on the duration of poor health at the end of life, thereby directly testing whether there was a linear relationship between the two and whether increasing survival led to an increase or decrease of the morbid period. Findings revealed that the morbid period was the longest among those who died in their late eighties while those who died early and those who survived into their nineties tended to have a shorter morbid period. This revealed that both compression and expansion were taking place in the same population, depending

on the length of survival. This has important implications for future public health research. Factors that promote life expectancy to the 90s seem to have the potential for compression whereas factors that promote life expectancy to the 80s seem to cause an expansion of morbidity. Further research should identify and delineate these factors so that public health interventions that promote compression of morbidity can be undertaken.

To summarize, these three projects have brought out certain important guiding principles that need to be followed in order to reduce the burden of terminal morbidity among older adults. To compress the morbid period, interventions among older adults should subscribe to the following tenets.

1. Preventive health behaviors can still be harnessed but control of chronic disease should be the primary focus
2. Diseases with low mortality and high disability risk need to be prioritized for control
3. Factors promoting survival beyond 90 need to be identified and promoted

In future, further research is planned to identify the factors that promote compression versus those that promote expansion of the morbid period. In the Cardiovascular Health Study, it is possible to identify baseline factors that promote survival to beyond 90 versus less than 90. Also, a cost effectiveness analysis to understand the impact of medical interventions like hip joint replacement on the morbid period will promote understanding of the interventions that may expand or compress the morbid period.

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